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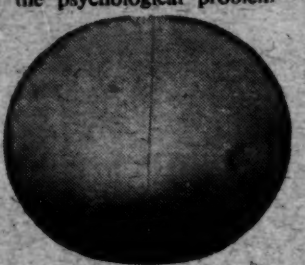

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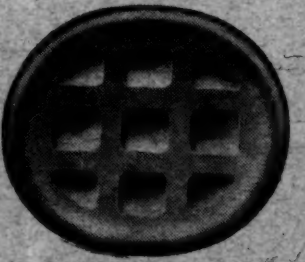

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 29 1952

SOME MEDICAL ASPECTS OF TOBACCO-SMOKING*

BY

RONALD BODLEY SCOTT, M.A., D.M., F.R.C.P.

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Of all the imports for which the Old World is indebted to the New, none equals in medical interest two which anticipated the Lease-Lend Act by nearly 450 years—syphilis and tobacco. It is of the second, the only drug to which addiction is universally considered respectable, that this paper treats.

Historical

So far as Western civilization is concerned, the history of tobacco begins on October 13, 1492, when Christopher Columbus landed on the island he named San Salvador. The natives sought to propitiate their visitors with rare gifts, including among them some dried leaves, which the Spaniards later threw away with smiles of condescension at the artless generosity of the savages. Nevertheless, within fifty years these leaves were eagerly sought in Europe, and were recommended for their medicinal properties by the French Ambassador at Lisbon, Jean Nicot, who later gave his name to nicotine. A century later the habit of pipe-smoking had firmly established itself in England. It survived the fulminations of James I, who published his *Counterblaste to Tobacco* within a year of coming to the throne, stigmatizing smoking as a "custome loathsome to the eye, hatefull to the nose, harmfull to the braine, dangerous to the lungs, and, in the black stinking fume thereof, nearest resembling the horrible Stygian smoke of the pit that is bottomlesse." The milder strictures of Charles II, who forbade Cambridge men to "wear periwigs, smoke tobacco or read their sermons," were equally ineffective. In Continental countries, where deterrents were more vigorous, the habit spread less rapidly: in Russia, smokers were discouraged by amputation of the nose, and in the Swiss Canton of Berne the offence was ranked as only one degree less odious than adultery. A prohibition against smoking in the streets was rigidly enforced by the police in Berlin up to 1848.

The habit has now become so universal that the occasional non-smoking compartment in railway carriages, which has long since replaced that formerly labelled "smoker," seldom contains more than one old lady. The increase has been due to the cigarette, a South American invention of the 1750's, which reached Europe through the Peninsula and was made fashionable by Louis Napoleon after the Crimean War. So vast has the consumption of tobacco become that the duty paid on it affords the Chancellor of the Exchequer one of his main sources of revenue, providing him in 1950 with £601,651,432. The moralist will find matter for reflection in the thought that over one-quarter of the country's income is now derived from the addiction of its inhabitants to tobacco and alcohol.

Much ingenuity has been expended in efforts to explain the attraction of tobacco-smoking. "I cannot imagine what pleasure they derive from this practice," wrote Oviedo in 1526, "unless it be the drinking which invariably precedes the smoking." He continues: "I am aware that some Christians have already adopted the habit, especially those who have contracted syphilis, for they say that in the state of ecstasy caused by the smoke they can no longer feel their pain." Of recent years less naive reasons have been postulated: the atavistic lure of fire worship, a pleasurable stimulation of the vagal nerve endings, and a rise in the blood-sugar level have all had their champions (Finnegan, Larsen, and Haag, 1945). The psychiatrists have made their characteristic contribution to the problem. "Getting something orally," one asserts (Bergler, 1946), "is the first great libidinous experience in life"; first the breast, then the bottle, then the comforter, then food, and finally the cigarette. More mundane, but perhaps better founded, is the suggestion that a true addiction to nicotine is at least part of the explanation (Finnegan, Larsen, and Haag, 1945; Johnston, 1942).

The Pharmacology of Smoking

The pharmacology of tobacco-smoking is more complex than at first appears; nicotine is the only alkaloid of importance in the leaf, but at least eleven others are recognized, although their biological actions are uncertain. Estimates of the quantity of nicotine entering the mouth during smoking vary: earlier reports claimed amounts as great as 3.6 mg. per cigarette, of which 90% was said to be absorbed (Pierce, 1941). More dependable assays are in the region of 1 mg. per cigarette weighing 1 g., 2.69 mg. per gramme of pipe tobacco, and 0.7–1.6 mg. per gramme of cigar (Ling and Wynn Parry, 1949). The proportion absorbed varies directly with the "wetness" of the smoker and inversely with the length of the cigarette-holder or pipe-stem. In the case of a cigarette smoked without a holder, it is estimated at about 0.5 mg., and this is borne out by comparing the antidiuretic effect of one cigarette with that of 0.5 mg. of nicotine given by injection (Burn, Truelove, and Burn, 1945). After smoking 20 cigarettes in seven hours the quantity of nicotine in the blood reaches an average of 0.14 mg. per litre; lower levels result from pipe or cigar

* A lecture delivered to the Bournemouth Medical Society on January 9.

smoking. It is remarkable that traces of nicotine can still be found in the blood ten hours after the last cigarette has been smoked (Wolff, Hawkins, and Giles, 1949).

Doses of 1–6 mg. of nicotine, by subcutaneous injection, are enough to produce such symptoms as sweating, faintness, tachycardia, nausea, and vomiting in non-smokers; much larger doses are tolerated by the habitué (Johnston, 1942). Nicotine's main effect is on the sympathetic nerve endings, first stimulating and later paralysing them. Cigarette smoke, however, contains a large number of other products, such as hydrocyanic acid, ammonia, carbon monoxide, pyridines, aldehydes, and tars. It is possible that the nausea and vomiting which occasionally assail the neophyte may be due to some of these substances. A man who habitually smokes 20 cigarettes a day absorbs enough carbon monoxide to maintain 5% of his haemoglobin in the carboxy form (Dixon, 1921).

Some observations on the mechanics of smoking are of interest. The average smoker consumes one cigarette in 17 puffs, with each of which he draws into his mouth 33 ml. of air; every 66 seconds he inhales the smoke, but by the time it has reached his lungs it has been diluted fifteenfold by the air in his respiratory passages (Fabricant, 1946).

The Physical Effects of Smoking

It is clear that the uses of tobacco and the effects of smoking upon the healthy and upon the diseased body must be a matter of close concern to our profession. The herb has, in fact, aroused medical interest ever since its introduction to Europe. It was for its medicinal virtues that it was cultivated in the sixteenth century, when, for a time, it enjoyed the reputation of a panacea. Application of tobacco leaves would heal a cancerous ulcer, it was claimed, and the apparently drowned were rapidly revived by insufflation of tobacco smoke into the rectum when they were suspended by the heels. It was widely used as a prophylactic against infection, and in 1665 the boys at Eton were given instruction in smoking, that they might ward off the plague; one pupil has recorded that he was never flogged so severely as when he refused his pipe.

Gradually attention shifted from the beneficent to the malignant effects of tobacco. The Victorian attitude accorded well with the view that any custom so enjoyable as smoking must of necessity be harmful; and in 1856 Mr. Samuel Solly was thundering at the students of St. Thomas's Hospital: "Now don't be frightened, my young friends, I am not going to give you a sermon against smoking, that is not my business; but it is my business to point out to you all the various and insidious causes of general paralysis, and smoking is one of them. . . . . I know of no single vice which does so much harm as smoking."

Much of the writing on the medical aspects of tobacco-smoking has come from the pens of non-smokers or of those who have renounced the habit and are basking in the sunshine of their own righteousness. For these reasons the appeal is often to the emotions rather than to the intellect. As recently as 1937, an English physician (J. D. Rolleston, 1937) wrote: "The three greatest statesmen of our time, Mussolini, Hitler, and Mr. Gladstone, did not smoke"; his paper closed with a plea to join the National Society of Non-Smokers and to subscribe to its journal, *Clean Air*.

This approach to the problem has made it difficult for us to offer our patients rational advice on the question, and I turn now to the consideration of some of the established facts regarding the effects of this habit. It has been proved that non-smokers live longer than smokers (Pearl, 1938), and that the decrease in survival is greater for heavy than for moderate smokers. Once the age of 70 years has been passed the harmful effects are no longer apparent. In another series (Short, Johnson, and Ley, 1938–9) the effect of smoking was investigated in 2,031 persons proposing for life assurance; 63.7% of these were habitual smokers and 24.4% had never smoked; the two groups were homogeneous in respect of age and sex. No differences in weight, blood pressure, or pulse frequency existed between them, but the smokers were more prone to colds in the head and complained more frequently of cough, palpitation, dyspnoea, and dyspepsia.

Its Effects upon the Cardiovascular System

It will be more profitable, however, for our present purpose to consider the various systems of the body and the effects tobacco is said to have on them. I begin with the cardiovascular system. Tobacco has a well-defined pharmacological action on the heart and blood vessels; the blood pressure shows a transient rise, averaging 15 mm. for the systolic and 10 mm. for the diastolic pressures; the pulse frequency increases by an average of 8 beats a minute; changes in the electrocardiogram, consisting of lowering, or even inversion, of the T waves, are frequent (Graybiel, Starr, and White, 1938; Stewart, Haskell, and Brown, 1945; Levy, Mathers, Mueller, and Nickerson, 1947). These disturbances are ephemeral and disappear when the cigarette is finished. Significant alterations occur also in the peripheral circulation: the skin temperature falls and the volume of the hand, as measured by the plethysmograph, diminishes (Lampson, 1935). These changes are undoubtedly the result of arterial narrowing, but it has been pointed out that a reflex peripheral vasoconstriction takes place whenever a deep breath is drawn and that inhalation alone might be responsible for the decrease in limb volume (Mulinos and Shulman, 1940). However, it has now been established that a progressive reduction in the volume of the limb occurs while cigarettes are being smoked, as well as the transient decrease which accompanies each inhalation (Shepherd, 1951). It must therefore be accepted that cigarette-smoking does lead to constriction of peripheral vessels, although it is possible that these effects are brought about by nicotine stimulating the release of adrenaline from the suprarenal glands (Short and Johnson, 1938–9).

These phenomena are, as I have stressed, manifestations of the pharmacological action of tobacco; it will be obvious that symptoms due to pre-existing cardiovascular disease may be aggravated by them, but there is no proof that tobacco initiates such disease. Nevertheless this contention is often made, and one or two specific instances must be considered. "Smoker's heart," an expression more familiar to our fathers than to us, was applied to a state in which premature contractions occurred in heavy smokers; it seems possible that this causal sequence is to be observed in some patients, but it is decidedly rare. It was regarded more seriously 45 years ago: tobacco might, it was said, "increase vascular tension and lead to tumultuous and forcible cardiac action"; persistence in the habit after these warnings might cause dilatation of the heart with very much more serious symptoms, which might even be fatal (Essex Wynter, 1907).

Attempts have been made to incriminate smoking as a cause of coronary artery disease, but in one series of 750 patients with angina the percentage of smokers was considerably lower than the percentage of non-smokers (White and Sharber, 1934). In another group of 1,000 men above the age of 40 years with evidence of coronary artery disease, 69.8% were smokers, while the figure for a control group without heart disease was 66.3%. Nevertheless, between the ages of 40 and 49 years 1% of non-smokers were found to have evidence of coronary artery disease, while in mild to moderate smokers the incidence was 4.6%, and in heavy smokers 5.9% (English, Willius, and Berkson, 1940). It is hardly necessary to point out that these observations do not imply a causal relationship: everyday experience suggests that the kind of man who has a coronary thrombosis before he is 50 is the kind of man one expects to smoke 25 cigarettes a day.

In some patients tobacco undoubtedly provokes anginal pain. In the majority there are convincing signs of disease of the coronary arteries, and smoking produces its effects by its action in raising the blood pressure and increasing the heart rate (Pickering and Sanderson, 1944–5). Very

occasional instances are recorded of what may with accuracy be called "tobacco angina": in one of these pain was provoked by smoking but not by exertion, there was no rise in blood pressure or heart rate, but transient changes in the ST segments of the electrocardiogram were noted. It was suggested that spasm of the coronary arteries induced by tobacco was responsible (Bryant and Wood, 1947).

The therapeutic deduction seems to be that patients in whom anginal pain follows smoking should be advised to abstain. There is not sufficient reason for forbidding all patients with angina to smoke, although a period of abstinence as a therapeutic trial is justifiable.

In the genesis of peripheral vascular disease tobacco has long been regarded as important. Every medical student reads in his textbooks that thrombo-angiitis obliterans occurs predominantly in chain-smoking Russian Jews. There is now dispute over the very existence of this disease; it is suggested that the name covers a multitude of pathological processes and that it is not to be distinguished from the senile variety of obliterative arterial disease (Boyd, Ratcliffe, Jepson, and James, 1949). It is still, however, the general belief that thrombo-angiitis obliterans is a specific morbid entity and that smoking is more dangerous in it than in senile obliterative arteritis. It has been claimed that occlusive vascular disease is more common in diabetics who smoke than in those who do not; in one series it was noted in 58% of smokers and in only 37% of non-smokers (Weinroth and Herzstein, 1946).

Although skin-sensitivity tests with extracts of cigarette smoke were reported as positive in 83% of patients with thrombo-angiitis obliterans and in only 10% of normals (Harkavy, Hebald, and Silbert, 1932–3), and although allergy to tobacco has been postulated as the basis of this complaint (Sulzberger, 1934), no evidence exists which convincingly incriminates smoking as a cause of this or any other peripheral vascular disease. Injections of nicotine into growing rats do not increase the incidence of arterial change (Thienes and Butt, 1938). The danger is due to the vasoconstrictor effects of tobacco, and there is unanimous agreement that sufferers from peripheral vascular disease should not smoke. It is not clear how much difference this interdiction makes to the elderly man with intermittent claudication; but when there is gangrene or the vitality of the skin is in doubt the ban should be absolute. The additional vasoconstriction may be enough to prevent healing or to precipitate death of tissue. One observer followed up 100 patients with thrombo-angiitis obliterans, who had ceased to smoke, over a period of ten years; in every case the disease was arrested (Silbert, 1945).

Its Effects upon the Respiratory System

In the respiratory system the irritant action of tobacco smoke might reasonably be expected to overshadow any systemic effects. We are all familiar with the patient who replies to our query with, "Just a smoker's cough, doctor," and, although he may have bronchiectasis, carcinoma of the lung, or pulmonary tuberculosis, a "smoker's cough" must be admitted. Tobacco smoke has a considerable local irritant action; a method of measuring this by the effect of six "standard puffs" of cigarette smoke in producing oedema of the rabbit's conjunctiva has been devised (Finnegan, Fordham, Larsen, and Haag, 1947). Researches show that different brands vary greatly in their irritant action, probably owing to substances added in the manufacture. Persistent heavy cigarette-smoking will certainly lead to a chronic pharyngitis and will keep alight chronic bronchitis in those predisposed. Apart from these obvious irritant effects, recent observations, showing that it reduces vital capacity and chest expansion, provide scientific justification for the belief that it is "bad for the wind" (Whitfield, Arnott, and Waterhouse, 1951).

Asthma due to tobacco must be very rare, although the case is recorded of a Turkish lady who was sensitive to cigars and was afflicted by asthma when she walked in the grounds of her estate, which adjoined a tobacco plantation (Urbach and Gottlieb, 1946).

In the past few years interest has been focused on the importance of smoking as a cause of carcinoma of the bronchus. The recorded mortality from this tumour in England and Wales increased fifteenfold between 1922 and 1947; it is now probably the commonest form of malignant disease met by the general physician. This increase has been noted in all countries of the Western World, with the exception of Iceland (Dungal, 1950); records show that bronchial carcinoma provides 27% of all malignant tumours in the post-mortem rooms of London (Bryson and Spencer, 1951) but only 2.9% in those of Reykjavik (Dungal, 1950). Cigarette-smoking has long been suspected as a cause, and some recent statistical investigations have proved this suspicion true. It is of interest, moreover, that the cigarette consumption in Iceland has been negligible until the last few years. In a series of 684 patients with bronchial carcinoma in the United States, only 1.3% were non-smokers and 51.2% had smoked more than 20 cigarettes a day for 20 years; the figures for these classes in the general hospital population without cancer were 14.6% and 19.1% (Wynder and Graham, 1950). Independent observations made in this country have led to the conclusion that after the age of 45 years those who smoke 25 or more cigarettes a day are fifty times more likely to develop carcinoma of the bronchus than non-smokers of the same age. No such correlation with pipe-smoking could be found (Doll and Hill, 1950).

The only known carcinogen in cigarette smoke is arsenic, but there is not enough evidence to inculpate it. It seems clear that some cause other than, or additional to, the increase in cigarette consumption must be sought to explain the increasing frequency of bronchial carcinoma, because the second has risen more rapidly than the first. It is difficult, moreover, to understand why there has been no parallel rise in the incidence of cancer of the upper respiratory tract, although carcinoma of the larynx and pharynx is significantly more frequent in smokers than in non-smokers (Schrek, Baker, Ballard, and Dolgoff, 1950).

The moral we should draw is obscure: perhaps we should caution all young men and women not to smoke more than 20 cigarettes a day. The popular reaction is illustrated by the subscriber to the *Readers' Digest* who was so upset by an article on smoking and cancer that he decided to give up reading magazines.

Its Effect upon the Alimentary Tract

To turn now to the alimentary tract: there is good reason for thinking that cancer of the lip is commoner in pipe and cigar smokers than in the general population, but this predisposition does not extend to cigarette smokers (Levin, Goldstein, and Gerhardt, 1950). Presumably local irritation must be held responsible.

The effect of smoking upon the stomach is of importance, because it has long been traditional to urge the patient with peptic ulcer to abstain. Smoking one cigarette has been shown to diminish hunger contractions and gastric motility as well as to decrease the volume and acidity of gastric secretion; in only one of twenty patients was there an increase in acidity. These effects are probably reflex, because they do not occur after injection of nicotine in dogs (Schnedorf and Ivy, 1939; Ivy, Grossman, and Bachrach, 1950). Wolf and Wolff (1943) were able to watch the behaviour of the stomach in their patient Tom, who had had a large gastric fistula for over forty years. When smoking was pleasurable no change took place in the gastric contractions, vascularity, or acid secretion; when he had no taste for it a cigarette induced slight nausea, contractions ceased, the mucosa became pale, and acid secretion failed; these changes were common to the sensation of nausea however evoked. The increase in appetite, which many who renounce smoking notice, may be due to the removal of the inhibitory influence of tobacco on gastric motility.

These physiological observations provide no theoretical justification for advising the patient with peptic ulcer to stop smoking, yet many physicians are convinced that tobacco has a deleterious effect on this disease. It is always said that the patient with peptic ulcer is a heavy smoker (Hurst and Stewart, 1929; Bockus, 1944), but in a careful survey it was found that men with chronic duodenal ulcer do not smoke, on an average, more than healthy men of the same age, although twice as many of them inhale (Trowell, 1934). Many experienced clinicians have noted dyspepsia, resembling that of ulcer, to disappear on abstinence from tobacco (Wagner, 1924; Bockus, 1944; Schindler, 1947). On the other hand, a careful follow-up of a group of patients with peptic ulcer (Jamieson, Illingworth, and Scott, 1946) revealed no correlation between alterations in tobacco consumption and variations in the severity of symptoms. Some figures suggest that the response to treatment with antacids is better if smoking is discontinued (Batterman and Ehrenfeld, 1949).

It seems fair to conclude that smoking plays no part in the genesis of peptic ulcer. That notoriously dangerous guide, "clinical impression," has led many to believe that it may aggravate symptoms. The sensible advice is to recommend patients to try a period of abstinence and decide for themselves whether they are better without their cigarettes.

There is some gastroscopic evidence that smoking may lead to changes in the gastric mucosa. In one series the appearances were normal in only 8% of heavy smokers, there was hypotrophic gastritis in 44%, and atrophic gastritis in a like proportion (Annis, 1944).

Cigarette-smoking has been observed to increase the motility of the large bowel in normal subjects (Schnedorf and Ivy, 1939), and this finding provides a physiological justification for Ryle's view (1928) that it is of importance in the causation of spastic colon. A period of abstinence is worth a trial in this disorder.

Its Effect upon the Nervous System

Many curious nervous disorders have been attributed to the use of tobacco. The French journals, in particular, contain numerous case reports: an officer's wife, afflicted with vertigo and signs of pyramidal tract disease, who recovered in two weeks after renouncing the 25 cigarettes she had smoked daily for fifteen years (Barré and Verdier, 1949); a myasthenic and polyneuritic syndrome in chewers of tobacco (Coulonjou, Prévot, Salaun, and Nicolet, 1946); a boy of 13 years who fell victim to the manic-depressive psychosis after smoking 20 cigars a day (Pel, 1911). These instances could be multiplied indefinitely; there are records of fleeting cerebral attacks, of neuralgic pains, of headaches, of fits, all lending support to Calverley's contention of

> How they who use fusees
> All grow by slow degrees,
> Brainless as chimpanzees,
> Meagre as lizards;
> Go mad, and beat their wives;
> Plunge (after shocking lives)
> Razors and carving knives
> Into their gizzards.

There was, however, one condition in which the role of tobacco seemed to be authentic. This was tobacco amblyopia, a disturbance of vision occurring chiefly in men between the ages of 35 and 55 years, starting as a paracentral scotoma for colours at the blind spot and gradually spreading to the point of central vision (Wilson, 1940). It was said to afflict particularly those who smoked strong shag (Moore, 1925). It was more common in the United Kingdom than in France or the United States, where alcohol had long been regarded at least as important as tobacco in its cause (Walsh, 1947). In one American series of 1,100 patients over the age of 50 years with this form of amblyopia, the average consumption of tobacco was less than in 500 healthy persons of the same age (Usher, 1927).

A correlation between malnutrition and the incidence of tobacco amblyopia has long been noted; de Wecker (Schepens, 1946) commented on its frequency during the siege of Paris in 1870, and a tenfold increase was observed under the German occupation of Belgium between 1940 and 1945. Carroll (1944) has reported complete or partial recovery in 25 patients with what he terms "tobacco–alcohol amblyopia" when their diets were supplemented with the vitamin-B complex or vitamin B_1 itself, although they continued to smoke and drink.

In this country alcohol lacks the importance accorded to it elsewhere (Evans, 1939), and tobacco is generally believed to be the essential cause, although malnutrition is allowed a predisposing role. The suggestion has been made that some unknown toxic substance is formed by fermentation in the heavier and darker tobaccos; this substance is rendered harmless by the healthy liver, but, when malnutrition impairs hepatic function, detoxication fails and the retina suffers (Evans, 1939; Schepens, 1946).

The similarity between amblyopia attributed to tobacco and that noted in malnourished prisoners of war (Denny-Brown, 1947) is obvious, but the resemblance is not exact. Proof that "tobacco" amblyopia is purely of nutritional origin is still lacking, and it remains wise to recommend patients with the complaint to abstain from smoking.

Its Effects upon the Genito-urinary System

The effects of tobacco on the genito-urinary system are not of great moment. In the normal man it has an antidiuretic action (Burn, Truelove, and Burn, 1945), due to nicotine provoking liberation of the antidiuretic hormone (Cates and Garrod, 1951). It was at one time believed to decrease libido and a Franciscan monk, Fra Giuseppe da Convertino, recommended it from personal experience as a safeguard for chastity. In more recent years it has been said to lead to abortion and infertility (Mgalobeli, 1931), although another authority asserts that he had found a group of pipe-smoking Frenchwomen, whose habits he had studied, to be of exceptional fertility (Chiasson, 1929).

It has been proved that nicotine is secreted in the milk in proportion to the number of cigarettes smoked; in heavy smokers the quantity may rise to 0.5 mg. per litre. Infants fed on this milk thrived normally, although they must have received 0.1–0.25 mg. of nicotine a day (Perlman and Dannenberg, 1942).

Conclusion

The public library in New York is said to contain more than 4,000 books on tobacco in more than 20 languages (Bishop, 1949). It will be appreciated, therefore, that a short paper can only touch the fringe of the subject. It is, however, a matter which closely concerns us as doctors, for patients are constantly asking our advice about smoking. Most of us are prepared to give it without deep reflection, for the view the doctor takes is dictated rather by the number of cigarettes he smokes himself than by a profound knowledge of the pharmacology of tobacco. It is, however, well to remember that some facts have now been established, and it should no longer be said that those of us who are heavy smokers impose no restrictions, while the non-smokers

> Compound for sins they are inclined to
> By damning those they have no mind to.

REFERENCES

Annis, J. W. (1944). *Gastroenterology*, **2**, 85.
Barré, M. J. A., and Verdier (1949). *Rev. neurol.*, **81**, 958.
Batterman, R. C., and Ehrenfeld, I. (1949). *Gastroenterology*, **12**, 575.
Bergler, E. (1946). *Psychiat. Quart.*, **20**, 297.
Bishop, W. J. (1949). *Brit. J. Addict.*, **46**, 49.
Bockus, H. L. (1944). *Gastro-Enterology*. Saunders, London.
Boyd, A. M., Ratcliffe, A. H., Jepson, R. P., and James, G. W. H. (1949). *J. Bone Jt Surg.*, **31B**, 325.

Bryant, J. M., and Wood, J. E. (1947). *Amer. Heart J.*, **34**, 20.
Bryson, C. C., and Spencer, H. (1951). *Quart. J. Med.*, **20**, 173.
Burn, J. H., Truelove, L. H., and Burn, I. (1945). *British Medical Journal*, **1**, 403.
Carroll, F. D. (1944). *Amer. J. Ophthal.*, **27**, 713, 847.
Cates, J. E., and Garrod, O. (1951). *Clin. Sci.*, **10**, 145.
Chiasson, M. J. (1929). *J. Amer. med. Ass.*, **93**, 1909.
Coulonjou, Prévot, Salaun, and Nicolet (1946). *Rev. neurol.*, **78**, 227.
Denny-Brown, D. (1947). *Medicine, Baltimore*, **26**, 41.
Dixon, W. E. (1921). *British Medical Journal*, **2**, 819.
Doll, R., and Hill, A. Bradford (1950). Ibid., **2**, 739.
Dungal, N. (1950). *Lancet*, **2**, 245.
English, J. P., Willius, F. A., and Berkson, J. (1940). *J. Amer. med. Ass.*, **115**, 1327.
Evans, P. J. (1939). *Trans. ophthal. Soc. U.K.*, **59**, 241.
Fabricant, N. D. (1946). *Amer. J. med Sci.*, **211**, 505.
Finnegan, J. K., Fordham, D., Larsen, P. S., and Haag, H. B. (1947). *J. Pharmacol.*, **89**, 115.
— Larsen, P. S., and Haag, H. B. (1945). *Science*, **102**, 94.
Graybiel, A., Starr, R. S., and White, P. D. (1938). *Amer. Heart J.*, **15**, 89.
Harkavy, J., Hebald, S., and Silbert, S. (1932-3). *Proc. Soc. exp. Biol., N.Y.*, **30**, 104.
Hurst, A. F., and Stewart, M. J. (1929). *Gastric and Duodenal Ulcer*. Oxford Univ. Press, London.
Ivy, A. C., Grossmann, M. I., and Bachrach, W. H. (1950). *Peptic Ulcer*. Churchill, London.
Jamieson, R. A., Illingworth, C. F. W., and Scott, L. D. W. (1946). *British Medical Journal*, **2**, 287.
Johnston, L. M. (1942). *Lancet*, **2**, 742.
Lampson, R. S. (1935). *J. Amer. med. Ass.*, **104**, 1963.
Levin, M. L., Goldstein, H., and Gerhardt, P. R. (1950). Ibid., **143**, 336.
Levy, R. L., Mathers, J. A. L., Mueller, A. A., and Nickerson, J. L. (1947). Ibid., **135**, 417.
Ling, H. W., and Wynn Parry, C. B. (1949). *Brit. J. Pharmacol.*, **4**, 313.
Mgalobeli, M. (1931). *Mschr. Geburtsh. Gynäk.*, **88**, 237.
Moore, R. Foster (1925). *Medical Ophthalmology*. Churchill, London.
Mulinos, M. G., and Shulman, I. (1940). *Amer. J. med. Sci.*, **199**, 708.
Pearl, R. (1938). *Science*, **87**, 216.
Pel, P. K. (1911). *Berl. klin. Wschr.*, **48**, 241.
Perlman, H. H., and Dannenberg, A. M. (1942). *J. Amer. med. Ass.*, **120**, 1003.
Pickering, G. W., and Sanderson, P. H. (1944-5). *Clin. Sci.*, **5**, 275.
Pierce, I. H. (1941). *J. Lab. clin. Med.*, **26**, 1322.
Rolleston, J. D. (1937). *Med. Pr.*, **195**, 443.
Ryle, J. A. (1928). *Lancet*, **2**, 1115.
Schepens, C. L. (1946). *Trans. ophthal. Soc. U.K.*, **66**, 309.
Schindler, R. (1947). *Gastritis*. Heinemann, London.
Schnedorf, J. G., and Ivy, A. C. (1939). *J. Amer. med. Ass.*, **112**, 898.
Schrek, R., Baker, L. A., Ballard, G. P., and Dolgoff, S. (1950). *Cancer Res.*, **10**, 49.
Shepherd, J. T. (1951). *British Medical Journal*, **2**, 1007.
Short, J. J., and Johnson, H. J. (1938-9). *J. Lab. clin. Med.*, **24**, 590.
—— —— and Ley, H. A. (1938-9). Ibid., **24**, 586.
Silbert, S. (1945). *J. Amer. med. Ass.*, **129**, 5.
Solly, S. (1856). *Lancet*, **2**, 641.
Stewart, H. J., Haskell, H. S., and Brown, H. (1945). *Amer. Heart J.*, **30**, 541.
Sulzberger, M. B. (1934). *J. Amer. med Ass.*, **102**, 11.
Thienes, C. H., and Butt, E. M. (1938). *Amer. J. med. Sci.*, **195**, 522.
Trowell, O. A. (1934). *Lancet*, **1**, 808.
Urbach, E., and Gottlieb, P. M. (1946). *Allergy*, Heinemann, London.
Usher, C. H. (1927). *Ann. Eugen., Camb.*, **2**, 245.
Wagner, F. (1924). *Med. Klin.*, **20**, 262.
Walsh, F. B. (1947). *Clinical Neuro-Ophthalmology*. Williams & Williams, Baltimore.
Weinroth, L. A., and Herzstein, J. (1946). *J. Amer. med. Ass.*, **131**, 205.
White, P. D., and Sharber, T. (1934). Ibid., **102**, 655.
Whitfield, A. G. W., Arnott, W. M., and Waterhouse, J. A. H. (1951). *Quart. J. Med.*, **20**, 141.
Wilson, S. A. K. (1940). *Neurology*. Arnold, London.
Wolf, S., and Wolff, H. G. (1943). *Human Gastric Function*. Oxford Univ. Press, London.
Wolff, W. A., Hawkins, M. A., and Giles, W. E. (1949). *J. Pharmacol.*, **95**, 145.
Wynder, E. L., and Graham, E. A. (1950). *J. Amer. med. Ass.*, **143**, 329.
Wynter, W. Essex (1907). *Minor Medicine*. Appleton, London.

During recent years industry has paid increasing attention to colour coding of danger points in factories to indicate high voltage lines, toxic gases, and obstructions such as low doorways and steps; the British Standards Institution considered the possibility of preparing a uniform "safety" colour code. However, following an inquiry by the Royal Society for the Prevention of Accidents it has now been decided to abandon the idea. Examination showed that a distinction must be made between a *safety* colour code and an *identification* code—the one being broadly to classify and give warning of types of hazard by colour and the other primarily to identify the contents of cylinders and so on. It was found that many colours had traditional meanings which were not reconcilable with their identification value—for instance, green CO_2 containers are not consistent with the concept of red for danger. Also, since anything up to 8% of the population is thought to be to some degree colour-blind, the application of a colour system can in no way be universally effective.

RETROLENTAL FIBROPLASIA

A PROBLEM OF PREMATURITY

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Retrolental fibroplasia may lead to blindness in infancy, and it is the gravity of this possible outcome that makes its study so urgent a problem. The disease has been the subject of a large number of papers in the American literature since Terry's first report (1942), in which he recognized it as a condition occurring in premature babies, leading to the formation of an opaque vascularized membrane behind the lens of both eyes, usually with gross visual defect and searching nystagmus. The subject has as yet received little attention in the medical press of this country, but there is reason to believe that the disease is making its appearance here in the same curiously uneven and unpredictable manner as in the United States and, more recently, in other countries.

A team drawn from the Oxford Eye Hospital, the paediatric department of the United Oxford Hospitals, and the Nuffield Laboratory of Ophthalmology has been concerned in a joint investigation since June, 1950.

Diagnosis of Cases

Early in 1950 we started routine ophthalmic examination of all premature babies of low birth weight born in Oxford, in the hope that some clue to the nature of the disease might be gained from observation of the condition as it developed, and later because of the possibility of treatment.

It is unlikely that retrolental fibroplasia occurs in infants weighing over 5 lb. (2.3 kg.) at birth, so this was our dividing line. All infants weighing 5 lb. (2.3 kg.) and under at birth are examined at the discretion of the paediatricians, larger and healthier children within a few days of birth, and small weakly babies, unable at first to tolerate the handling involved in an ophthalmic examination, after several weeks. After the first examination infants are seen every week while in hospital. They are usually discharged on reaching a weight of 5 lb. (2.3 kg.) and are then followed up at special clinics at the Eye Hospital. Generally a baby will be seen fortnightly until it is between 3 and 4 months old, and then monthly until 6 months of age, when it is discharged from supervision if no signs of the disease have appeared. If any suspicious feature is seen in the eyes, particularly retinal vascular dilatation of marked degree, the infant may be examined at shorter intervals.

The examinations are all made by an ophthalmologist, and the infant is held by a nurse experienced in this work. General anaesthesia is unnecessary, though a comforter is invaluable. The pupils are dilated with

homatropine 1% combined with cocaine 2% instilled into the eyes half to one hour before examination, and repeated if necessary. It is almost always possible to see far out to the retinal periphery; on two occasions only have we found it necessary to steady the eye with conjunctival fixation forceps, after using a drop of local analgesic.

There are certain differences between the ophthalmological appearances of the infantile and the adult eye. Unless these are appreciated confusion is likely. The infantile optic disk is always extraordinarily pale and the central fundus often has a patchy distribution of pigment. The retinal periphery constantly has a peculiar oedematous-looking greyness, gradually merging into the pinkness of the posterior fundus. These appearances have been seen in both full-term and premature babies, and they gradually disappear during the first weeks of life.

Early diagnosis of the disease is not easy. Many of the preliminary stages seem to develop gradually from conditions which are apparently normal in the infant. The grey zones in the retinal periphery appear to be a constant feature of the infantile eye. Only observation week by week, or even from day to day, makes it possible to be sure that this appearance is normal and not increasing.

The periphery of the infant lens is often doubly refractile, and this may lead one to suspect a detachment of the retina when in fact there is none. We are sure that diagnosis of the disease cannot be made without the presence of a retinal detachment or thickening, or of some retrolental mass near the periphery. In addition to these signs engorgement of the retinal vessels and formation of "fans" of new vessels from the retinal vessels, often coming forward into the vitreous in front of the thickened or detached retina, are important diagnostic points. We do not regard retinal vascular dilatation alone as sufficient to warrant a diagnosis of retrolental fibroplasia.

Treatment with A.C.T.H.

Reports of the results of treatment with A.C.T.H. and cortisone show no general agreement. The small number of cases in the series treated and the unpredictable course of the disease make evaluation of treatment difficult. The organization of vitreous opacities is probably responsible for the final cicatricial changes, and it is in preventing the formation of this fibrous tissue that A.C.T.H. may be expected to exert its effects. In Woods's (1950, 1951) experience with 10 treated cases, the results of the use of A.C.T.H. were unfavourable. Fitzgerald *et al.* (1951) treated three cases with A.C.T.H., with unfavourable results, and three cases, in the late glaucomatous stage of the disease, with cortisone locally, with results of doubtful significance. On the other hand, the experience of Reese and Blodi (1951a) has encouraged them to continue the use of A.C.T.H. In 14 of their treated cases the disease either regressed or was arrested, while the disease progressed in six out of the eight untreated cases under their care during the same period. Scheie *et al.* (1951) treated five cases, and concluded that treatment with A.C.T.H. is worth further trial.

In a personal communication from Dr. Perera and Dr. Day, of New York, in November, 1950, we learned of their early experience with A.C.T.H. We were fortunate in obtaining a supply of the drug for treatment of a case in December, 1950. Since then five further cases have been treated.

We gave A.C.T.H. by intramuscular injection to the six cases in four doses daily, totalling 20–25 mg. When reactions caused anxiety, each dose was divided and given in two parts with a 10-minute interval. In three cases the drug was discontinued temporarily when the baby's condition was unsatisfactory, and treatment was restarted without causing any further ill effects. When the ophthalmologist considered the disease to be quiescent the dose was usually halved for two or three days before discontinuing treatment. The infant was then kept in hospital for a further period of at least eight days under the closest supervision, and subsequently followed up in the out-patient department. In no case has there been any relapse after discharge from the ward.

In our first case we were afraid of the possibility of relapse with rapid development of blindness on stopping the drug, and continued it very much longer than we would now consider necessary, giving a total of 1,025 mg. over 76 days. In the other five cases the duration of treatment varied from 22 to 39 days and the total dosage of A.C.T.H. was 300 to 620 mg.

Complications Arising During Treatment

Intercurrent Illness.—Hospitalization of these small premature infants is a serious responsibility, and strict barrier nursing in isolation cubicles is essential if they are to be treated in a children's ward. Three babies remained well throughout treatment, and the other three were ill at some time.

Immediate Reactions.—Transitory blanching of the infant may occur within one or two minutes of the injection, the condition passing off in less than 10 minutes.

Hypertension.—There has been moderate or severe hypertension in five of the six cases treated, and the systolic pressure has been extremely labile. The degree of hypertension has not followed the dose of A.C.T.H. closely, and in cases in which the drug has been stopped temporarily the hypertension has not necessarily returned on resuming the original dose. In three cases the pressure has reached 180–200 mm. Hg, and in two it has risen to 280–300 mm. Hg, on one or two occasions without any apparent change in the infant's condition. Hypertension is presumably due to impurities in the A.C.T.H., but we have not found it vary with the batch of drug in use. Our colleagues in New York had not mentioned it as a complication. We found some consolation in the fact that the infant's vessels are elastic and in the well-recognized observation that the small infant with pink disease can support a moderate degree of hypertension for several months with no apparent after-effects. Since treatment was stopped the blood pressure in all cases has returned to normal.

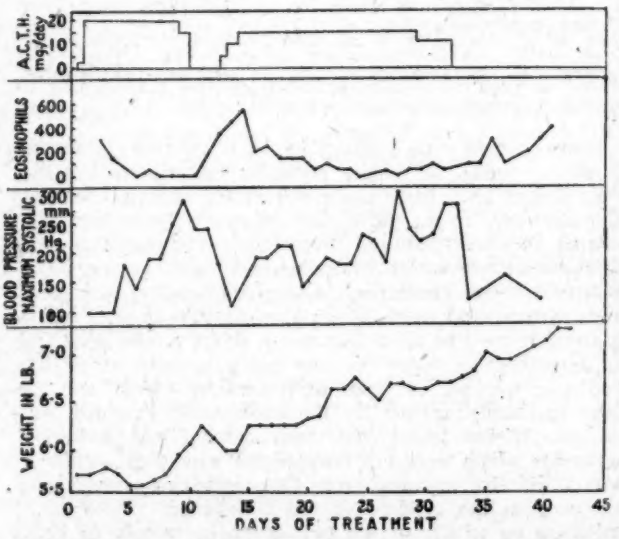

FIG. 1.—Records of A.C.T.H. dosage, eosinophil count, blood pressure, and weight in Case 4.

Electrolyte Balance.—As Dr. Day led us to expect, we have had remarkably little trouble and have not been able to ascribe any symptoms to changes in the electrolyte balance. In our first case blood was taken at frequent intervals for sodium and potassium estimation, but this was abandoned as causing unnecessary trauma. In subsequent cases we have relied upon electrocardiograms taken at weekly intervals. When the E.C.G. suggested a potassium deficiency we have given potassium in the form of potassium chloride, 0.5 g. daily in four divided doses by mouth.

Weight.—A rapid gain in weight may indicate water retention, but in only one of our cases did a transitory retention seem likely. Several infants gained little during treatment and rapidly improved immediately the drug was discontinued. The only infant who made a very satisfactory gain throughout was the one in whom hypertension never developed. In no case have we as yet encountered any complication which has persisted after treatment has been discontinued. Fig. 1 shows A.C.T.H. dosage in detail and its effect on the eosinophil count, blood pressure, and weight in one of our cases.

Case Histories

Case 1.—A boy, weighing 3 lb. 2½ oz. (1.4 kg.) at birth, was the first child of a 38-year-old mother who had severe toxaemia of pregnancy superimposed on chronic renal disease. Delivery was by caesarean section at 37 weeks. When the child was 2 months old many small retinal haemorrhages were seen. At 3 months there were retinal detachments in both nasal and temporal quadrants of the right eye, with new-vessel formation on the surface of the retina, and a vitreous opacity in front of this. The left eye seemed normal. During the next few days the condition of the right eye worsened rapidly and the baby was admitted to hospital for treatment with A.C.T.H. Next day the left eye showed an early detachment of the retina, and this progressed despite treatment. The right eye developed bands, or folds, in front of the detached retina, somewhat similar to the appearance of retinitis proliferans. Eventually the right retina became completely detached and a dense retrolental membrane developed. The left eye showed a grey mass of retina in the temporal quadrant, with a vitreous veil in front of it. There was nystagmus and the child did not follow a light. As the condition in the left eye seemed stationary, treatment was stopped after 76 days. We now consider this period too long, and it has been reduced in later cases. Six months after treatment ended the condition was unchanged, though the anterior chamber in the right eye was shallow. Nystagmus was less marked and the child picked up small objects, had a useful visual field, and was developing normally.

Case 2.—A girl, one of non-identical twins, the other child being normal, was born by spontaneous labour at the 33rd week and weighed 3 lb. 10 oz. (1.6 kg.). The neonatal period was complicated by bronchopneumonia, which responded to penicillin and streptomycin. At 6 weeks of age retrolental fibroplasia was diagnosed. Both eyes showed gross arterial and venous dilatation spreading out to the periphery, with many visible capillaries and a few small haemorrhages, and there was a retinal detachment on the left. Treatment by subconjunctival and oral administration of cortisone was tried. After a week of this treatment, when the child had received 1.5 mg. cortisone by injection and 150 mg. by mouth, the retinal condition showed no sign of diminishing activity and the right eye developed a peripheral detachment. A.C.T.H. was then substituted for cortisone. At this time there was gross vascular engorgement in each eye, with a few small retinal haemorrhages and peripheral detachments of the retinae. These vascular changes were more marked in the left eye. Vitreous opacities appeared in the right eye. When the stage of active vascular dilatation was over, a retinal fold developed, running from the retinal detachment to the optic disk and obliterating the right macular region. The retina in the left eye became completely detached. When the child was seen at 9 months of age the left eye showed a complete retrolental membrane, and the right eye a retinal fold, but the child takes an interest in her surroundings and can see small objects.

Case 3.—A girl, birth weight 4 lb. 6½ oz. (2 kg.), 33 weeks' gestation. The mother had severe toxaemia a week before the child was born after induction of labour. At 3 weeks of age the child was found to have engorged retinal vessels, but the peripheral grey areas were within normal limits. At 5 weeks a small detachment had appeared in the right eye and treatment with A.C.T.H. was begun. Within the next 10 days, despite treatment, the detachment had become more definite in the right eye and there were signs of activity in the left. The vascular engorgement lessened and the detachment did not increase after the child was 8 weeks old. Treatment was stopped, and the ocular condition has remained unchanged. When the child was 8 months old the central fundi of both eyes were normal; in the left eye there was marked greyness in the temporal periphery. She has good vision.

Case 4.—A boy, birth weight 3 lb. 15 oz. (1.8 kg.), gestation 36 weeks, labour spontaneous. A diagnosis of retrolental fibroplasia was made when the child was 6 weeks old because of a typical vitreous opacity and dilated vessels, with an apparent retinal detachment, in the temporal half of the right eye. Treatment was begun and for the next few days no change occurred. At 8 weeks of age a tongue of vitreous haze was seen on the extreme nasal side of the right eye and there was vascular dilatation behind this. In the left eye there was increased tortuosity of vessels and new-vessel formation on the edge of the temporal grey zone. At 9 weeks there seemed to be a definite detachment behind the vitreous haze in the right eye, whilst the left eye had a suspicious area in the inferior quadrant of the globe. There was no nystagmus, and the child seemed to follow a light. At 11 weeks all that could be seen to be abnormal was a small tongue of detached retina in the extreme nasal periphery in the right eye, whilst in the left there was no detachment or dilated vessels. Treatment was stopped when the child was 13 weeks old, as there had been no further changes in the retinae for the previous few days. The vitreous opacity in the right eye has remained much as it was, but the retinal detachment seemed to have become less. The changes in the periphery of the left eye consisted of the presence of a large grey zone in the retina. When 9 months old the child could obviously see well; in the right eye the detachment was still present but flat, and no gross abnormality was seen in the left eye.

Case 5.—A boy, birth weight 3 lb. 4 oz. (1.5 kg.). His mother was a primipara aged 17; she had toxaemia of pregnancy, and surgical induction was performed for this; normal labour followed. An upper respiratory infection in the child was treated by chemotherapy. At 5 weeks the upper temporal vessels were dilated and tortuous in the left eye and many vessels were dilated at the edge of the grey zone; at least one haemorrhage was seen. The right eye showed similar but less obvious changes. Three days later a detachment in the left temporal periphery could be seen and the grey zones of the right eye had become more extensive. Because of these changes a diagnosis of retrolental fibroplasia was made and treatment with A.C.T.H. begun. The condition remained active in both eyes and a vitreous haze appeared, partly hiding the detachment in the right eye; the detachment in the left eye became more extensive and the vessels very dilated; there was a fresh haemorrhage in the right eye. Two weeks later the disease appeared stationary. A curious feature observed at this stage was a red patch in the middle of the detached area; this appeared to be a hole through which one could see the choroid. In another week the vasodilatation had disappeared and treatment was stopped. When last seen (at 13 weeks old) no further change had taken place, but the retinal detachments were flatter. The central areas appeared to be normal. At 7 months scarring was present in the

peripheral retinae of both eyes, and the left eye was probably becoming myopic. The child takes an interest in his surroundings and picks up objects.

Case 6.—A girl, birth weight 2 lb. 6 oz. (1.1 kg.); born by caesarean section. Apart from a scalp laceration during the operation and an attack of vomiting and abdominal distension which responded to chemotherapy, the neonatal period was uneventful. At 10 weeks, on routine ophthalmological examination it was noticed that there was vasodilatation, more marked on the following day, and that a shallow retinal detachment was present in the periphery of both eyes. The infant was given A.C.T.H. for 10 days. The disease made no further progress and the detachments became flatter. She has been examined several times since, and, apart from a shallow retinal detachment or thickening in the periphery of the upper temporal quadrant of the right eye, the eyes appeared normal; there was a large grey zone in the left eye, but no detachment. When 10 months old this child proved difficult to examine, but both fundi appeared to be within normal limits, and the child could see well.

Comment on Untreated and Treated Cases

Untreated Cases.—The early cases were all in a late stage of the disease when first seen. In one of them the process had apparently been confined to one eye, but in 15 it was bilateral. The degree of visual defect varied. In those children in whom there was a complete retrolental membrane with total detachment of the retina, gross nystagmus was present and there was no perception of light. In others, useful vision has been retained, despite the presence of peripheral retinal detachment. Such vision as has been retained is not commonly central, but is adequate to enable the child to avoid obstacles. On the other hand, central visual acuity may be good. This frequent preservation of useful vision makes it essential that these eyes should not be removed simply in order to confirm the diagnosis. The clinical picture, taken in conjunction with the history, is characteristic.

A further six cases were seen early enough to permit A.C.T.H. treatment, and they are described in some detail below.

Cases 1 and 2 had a florid active type of the disease, which we should have expected to proceed to the full development of retrolental membrane and complete retinal detachments in both eyes. Our impression was that after treatment the disease was arrested at an earlier stage than would have been expected without treatment. We are aware, however, that this is often a self-limiting disease, and have seen two untreated cases in which one eye did not develop the disease to the full extent.

Cases 3, 4, 5, and 6 were diagnosed earlier than the first two, and treatment started immediately. The disease settled fairly quickly, and after the eyes became quiet no further deterioration occurred. It may be that we were dealing with a milder form of the disease, as variation in the severity is known to occur, but it is a fact that these cases showed fairly steady improvement after the use of A.C.T.H.

Though no definite conclusion can be drawn from this small series, the following comparison can be made between the results of the disease in babies born during the year preceding the use of A.C.T.H. and the results of treatment with A.C.T.H. In the former group three children were totally blind; three were partially blind, retaining sufficient vision to avoid large objects; and another child, who has now left this area, is expected to have good vision in one eye. In the latter group only two complete retrolental membranes developed, and no child was totally blind.

Pathology

We agree with those (Reese, 1948; Kinsey and Zacharias, 1949) who believe that the increased incidence of retrolental fibroplasia cannot be completely explained by the recent improvement in survival rate among infants of low birth weight. Confusion has been caused by the suggestion that we may be dealing, not with one disease, but with several, the final result of each of which is the formation of opaque tissue behind the lens. Another possibility is that the disease itself is changing in character, for the description by Terry (1948) differs widely from more recent ones (Owens and Owens, 1949; Hepner, Krause, and Davis, 1949; Reese and Blodi, 1951a).

Vascular Basis

Terry (1948) described the first evidence of the disease as a dot-like opacity occurring behind the lens and spreading outwards towards the periphery. This spread, in Terry's view, is associated with a reopening of the hyaloid vessels and consequent vascularization of the retrolental membrane.

The hyaloid vessels were also thought to be involved in the disease by Reese and Payne (1946), who described cases

FIG. 2.—Fibrovascular connective tissue membrane behind lens Complete retinal detachment extending beyond ora serrata Subretinal exudate.

of "hyperplasia of the primary vitreous with persistence of the tunica vasculosa lentis." These authors considered the condition to occur antenatally in either premature or full-term babies. They also state that the retina in these eyes may or may not be in position. This does not agree with our experience and that of many others, in which the condition of retrolental fibroplasia as it now occurs is of post-natal development and associated, in the fully developed case, with a totally detached retina; these eyes are ophthalmoscopically normal at birth and for a variable period afterwards. Unsworth (1948) also concluded that the disease was post-natal and suggested that the anaemia of prematurity was the cause. Reese (1949) and Klien (1949) reported further cases, reiterating their belief that the matrix of the disease was present at birth and angiomatous in nature.

Lately the part the retinal vessels themselves play in the development of the disease has been increasingly stressed, and our experience supports this change of emphasis. Owens and Owens (1949) and Reese and Blodi (1951a) have described the early stages of the disease as characterized by vascular dilatation on the retina, exudation into the vitreous, and the development of a peripheral detachment of the retina. Others (Laupus and Bousquet, 1951) regard the

occurrence of retinal haemorrhages as an essential part of the picture, but these have occurred in only a few of our cases. Reese and Blodi (1951a) have convincingly shown the early involvement of the retinal vessels in the disease process.

It is possible that an exudative choroido-retinitis causes a retinal detachment, which sets up a cyclitis with the formation of a retrolental membrane (Fig. 2). The retinal detachment may be due to a developmental defect (Wolff, 1950; Dixon and Paul, 1951). These authors have put forward evidence that a retinal separation has occurred in the pars ciliaris retinae of eyes in which the disease develops.

Associated Abnormalities.—Whether or not retrolental fibroplasia represents a generalized abnormality of neuro-ectodermal structures is a question which still remains to be answered. Krause (1946) was convinced that this was so and that the ocular changes were merely a part of what he called "encephalo-ophthalmic dysplasia" which led to mental retardation as well as gross visual defect.

It is difficult to assess the mental development of a very young child handicapped by blindness, but mental abnormality in these children has not been stressed by most writers. In some of our cases mental development has been slow, but we feel it is too early yet to assess the ultimate intellectual capacity of the children.

Sex Incidence and Multiple Births.—Speert, Blodi, and Reese (1950) analysed a series of 104 cases and found the sex incidence approximately equal. In Oxford 9 out of 22 cases were twins, but Kinsey and Zacharias (1949), in their larger series, could find no correlation between multiple births and the incidence of retrolental fibroplasia.

Antenatal and Post-natal Factors

American workers have concluded that the mother's age, race, parity, and rhesus group are not related to the development of the disease. There is no evidence that toxaemia of pregnancy, antenatal bleeding, drugs used in pregnancy or labour, or the cause of the premature labour are significant. It has not been possible to correlate the incidence of any chronic disease in the mother with the development of retrolental fibroplasia. Speert, Blodi, and Reese (1950) report two cases in which the disease had followed maternal rubella in the first three months of pregnancy, but no other known bacteria or virus has been implicated.

One of the first post-natal factors to be investigated was the effect of light on the immature retina. Hepner, Krause, and David (1949) covered the eyes of five babies weighing 3 lb. (1.4 kg.) or under at birth, for up to 60 days of life. Four babies developed retrolental fibroplasia, while the fifth remained normal.

Owens and Owens (1949) state that vitamin E is deficient in the newborn rat, and that the deficiency might be enhanced by a reduced fat diet and by the administration of vitamin A and iron. They gave 150 mg. of α-tocopherol acetate orally each day, and reduced amounts of vitamin A and iron, to 23 infants of 3 lb. (1.4 kg.) or less at birth. Of these, only one baby developed retrolental fibroplasia. In a control series of 78 infants of 3 lb. (1.4 kg.) or less, 17 babies developed the disease. In nine early cases vitamin E was given and the lesion was arrested in five of them. Unfortunately this work has not been confirmed. In Oxford during 1950–1 five infants developed retrolental fibroplasia while having vitamin E in the form and dosage suggested by Owens and Owens.

No known post-natal infections play a part in the aetiology of retrolental fibroplasia, but it is possible that some unknown infective agent may be responsible.

In looking for a recent change in treatment which might be held responsible, oxygen was considered, for modern oxygen cots and tents permit a very high concentration of the gas. Kinsey and Zacharias (1949) found that babies developing retrolental fibroplasia had been treated for a significantly longer period in oxygen than those who remained normal. Campbell (1951) found a significantly higher number of cases in a hospital where oxygen was freely used than in a second hospital where the use of oxygen was limited. It is doubtful, however, whether the two series are comparable. One baby in our series who had received no oxygen developed the disease, and in other centres where oxygen is used freely no cases have occurred. The importance, if any, of delayed feeding in the handling of small babies is obscure.

Incidence

Retrolental fibroplasia was reported in the United States 10 years ago, but so far as can be assessed it has appeared in England more recently. Reese and Blodi (1951b) report 272 cases studied at the Institute of Ophthalmology in New York; 236 of these were diagnosed during and after 1944. In Boston also the increase has been considerable. The disease is unevenly distributed amongst the various American centres. Exline and Harrington (1951), from New Orleans, report 80 infants under 3 lb. 5 oz. (1.5 kg.) at birth over a two-year period ending December, 1948, amongst whom no case of retrolental fibroplasia was found: 80% of these children were negroes.

From Paris, Lelong (1951) reported 44 cases during the period 1948–50. Campbell (1951) reported 27 cases from Melbourne. In England the first cases were reported by Martin and Franklin (1949), Moffatt (1950), Crosse (1950), and Minton and Cole (1951). It is known that cases are being diagnosed in other centres in England and that the number of cases is increasing.

In Oxford eight cases were diagnosed in 1949, representing 3.8% of surviving premature babies. In 1950 there were five new cases, and up to the end of June, 1951, four babies had developed the disease.

During 1950, Dr. Alison Webb, of the Children's Department, investigated the causes of blindness among pre-school-children in Oxfordshire, Berkshire, and Buckinghamshire. Although the numbers are very small, in 1950 retrolental fibroplasia was the largest single cause of blindness among these children.

An attempt was made to examine all babies weighing 4 lb. (1.8 kg.) or under at birth born or treated in the Oxford hospitals over the period from 1946–50. Of these children, 88% were traced and no signs of the disease were found in these.

Summary

Retrolental fibroplasia is a disease of recent appearance in Great Britain. It is confined to premature infants of low birth weight, is of post-natal appearance, and may lead to gross visual defect or blindness of both eyes.

Since 1947, 22 cases have appeared in Oxford. Their diagnosis is discussed.

The method, results, and side-effects of treatment of six cases with A.C.T.H. are given. It is considered that the disease was restrained by this treatment.

Despite gross intraocular damage, many of the eyes retain sufficient vision to enable the child to avoid obstacles and to walk about unaided. Excision of the eye is unnecessary, and is to be avoided in view of this possibility.

The aetiology and pathology of the disease are briefly discussed. Its cause remains unknown.

We should like to thank Mr. J. P. F. Lloyd and Mr. Victor Purvis, of Oxford, and Mr. R. C. Williams, of Aylesbury, for permission to publish the details of some of these cases; also the obstetricians of the United Oxford Hospitals for their constant and ready help, and Mrs. A. Pirie for advice. Our thanks are also due to the sisters and nursing staff of the United Oxford

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REFERENCES

Campbell, K. (1951). *Med. J. Aust.*, 2, 48.
Crosse, V. M. (1950). *Proc. roy. Soc. Med.*, 43, 232.
Dixon, J. M. and Paul, E. V. (1951). *Amer. J. Ophthal.*, 34, Special No. 5, pt. 2, p. 182.
Exline, A. L., and Harrington, M. R. (1951). *J. Pediat.*, 38, 1.
Fitzgerald, J. R., Bellows, J. G., Donegan, J. M., Gamble, R. C., Krause, A. C., Mann, W. A., Pearlman, M. D., and Zekman, T. N. (1951). *Arch. Ophthal., Chicago*, 45, 320.
Hepner, W. R., Krause, A. C., and David, M. E. (1949). *Pediatrics*, 3, 824.
Kinsey, V. E., and Zacharias, L. (1949). *J. Amer. med. Ass.*, 139, 572.
Klien, Bertha A. (1949). *Arch. Ophthal., Chicago*, 41, 553.
Krause, A. C. (1946). Ibid., 36, 387.
Laupus, W. E., and Bousquet, F. P. (1951). *Amer. J. Dis. Child.*, 81, 617.
Lelong, M. (1951). Unpublished lecture.
Martin, J. K., and Franklin, A. W. (1949). *Proc. roy. Soc. Med.*, 43, 235.
Minton, J., and Cole, P. (1951). *British Medical Journal*, 1, 450.
Moffatt, P. McG. (1950). *Proc. roy. Soc. Med.*, 43, 223.
Owens, W. C., and Owens, E. U. (1949). *Amer. J. Ophthal.*, 32, 1, 1631.
Reese, A. B. (1948). Ibid., 31, 95.
—— (1949). *Arch. Ophthal., Chicago*, 41 527.
—— and Blodi, F. C. (1951a). *Amer. J. Ophthal.*, 34, 1.
—— —— (1951b). In A. Sorsby's *Systemic Ophthalmology*, p. 14. Butterworth, London.
—— and Payne, F. (1946). *Amer. J. Ophthal.*, 29, 1.
Scheie, H. G., Tyner, G. S., Buesseler, J. A., and Alfano, J. E. (1951). *Arch. Ophthal., Chicago*, 45, 301.
Speert, H., Blodi, F. C., and Reese, A. B. (1950). *Amer. J. Obstet. Gynec.*, 59, 246.
Terry, T. L. (1942). *Amer. J. Ophthal.*, 25, 203, 1409.
—— (1948). *Advanc. Pediat.*, 3, 55.
Unsworth, A. C. (1948). *Arch. Ophthal., Chicago*, 40, 341.
Wolff, E. (1950). *Proc. roy. Soc. Med.*, 43, 227.
Woods, A. C. (1950). *Amer. J. Ophthal.*, 33, 1325.
—— (1951). Ibid., 34, 945.

DEPRESSION OF TUBERCULIN SENSITIVITY IN GUINEA-PIGS BY CERTAIN ANTITUBERCULOUS SURFACE-ACTIVE AGENTS

BY

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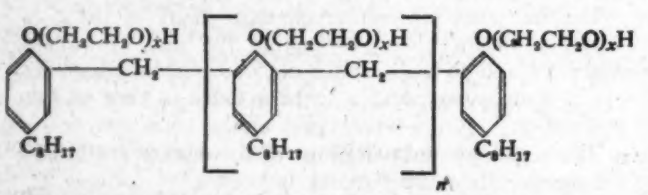
Substances known to depress skin sensitivity to tuberculin are few in number (Long and Miles, 1950; Fisher, Harington, and Long, 1951; Long, Miles, and Perry, 1951c), and when such depression is associated with anti-tuberculous action the question arises whether the chemotherapeutic mechanism is the same as, or is allied to, the anti-allergic.

The development of experimental tuberculosis in mice was shown by Cornforth, Hart, Rees, and Stock (1951) to be markedly inhibited by the injection of non-ionic, water-soluble, surface-active polyoxyethylene ethers of



n=0, 1, 2, 3, and higher integers. x=10, 20, or 60 (average value).

low toxicity, having the general formula given here, and obtained by polymerization of ethylene oxide with condensation products of formaldehyde with *p-tert*-octyl phenol. The antituberculous effect of these detergents has since been confirmed in the guinea-pig, in which a substantial curative action was shown in an established (three-weeks-old) infection. Routine quantitative tuberculin tests made at the end of a 60-day course of treatment showed a marked reduction in hypersensitivity in the detergent-treated animals as compared with their controls. The desensitization appeared to be specific rather than due merely to suppression of tuberculosis, since it was more evident than in a parallel group of streptomycin-treated animals with somewhat greater suppression of disease. This unexpected observation has led us to a more precise study of the depression of tuberculin sensitivity by these agents in B.C.G.-sensitized guinea-pigs, using the method of Long and Miles (1950). We hoped to see whether this action resembled that of other substances known to diminish tuberculin allergy, and whether it was related to antituberculous activity.

Materials and Methods

Surface-active Agents.—Representative members of the series (see formula) were used (average of 20 units of ethylene oxide per phenolic nucleus, unless otherwise stated). These were D2, a mixture of compounds having various values of n from 0 upwards; D2a, a similar mixture but with a smaller proportion of the lower members of the series; D9a, an isolate with n=1 ("triplet"); D14, a mixture like D2 but with 10 units of ethylene oxide per phenolic nucleus, and therefore less hydrophilic; D22, a mixture like D2 but with an average of 60 units of ethylene oxide per phenolic nucleus, and therefore more hydrophilic. Compounds D2, D2a, and D14 were chemotherapeutically active in the tuberculous mouse; D9a and D22 were inactive. The compounds were synthesized by our colleagues, Dr. J. W. Cornforth and Mr. J. A. Stock. They were given intravenously in 0.5 ml., or subcutaneously in 1 ml., saline.

Cortisone was given as the acetate (Merck), subcutaneously in 1 ml. normal saline.

Guinea-pigs.—The Hampstead strain of albinos was used, the animals weighing about 350 g. They were fed on a pelleted diet (Bruce and Parkes, 1947) supplemented, unless otherwise stated, with unlimited cabbage. B.C.G.-sensitization was carried out as described by Long and Miles (1950).

Tuberculin Sensitivity.—This was tested by intracutaneous injections of 32 and 320 international units of O.T. in 0.2 ml. saline.

Effect on Tuberculin Sensitivity

The intravenous route was considered most likely to reveal any differences between the surface-active agents, since variations in absorption would be excluded. Intravenous injection of the chemotherapeutically active preparations D2, D2a, and D14 in doses of 10 mg. in the B.C.G.-sensitized guinea-pigs, immediately before tuberculin injections, produced a significant though limited diminution of sensitivity as compared with untreated sensitized controls; the diminution was of the same order as that produced by cortisone 2 mg. given subcutaneously six hours before the tuberculin. On the other hand, the chemotherapeutically inactive D9a and D22 were without appreciable effect in these intravenous doses, and even at 25 mg. (this dose, in the case of D22, being chosen so as to contain the same weight of phenolic nuclei as 10 mg. of D2—see above).

The desensitizing properties of D2a were further examined, choosing the more convenient subcutaneous route, injections being given in groups of ten B.C.G.-sensitized guinea-pigs two hours before the tuberculin. Under these conditions D2a gave its maximal effect on tuberculin depression, in comparison with the controls, at doses of 100 to 10 mg., there being no significant difference from the effect of cortisone 2 mg.; D2a had no effect at 1 mg.

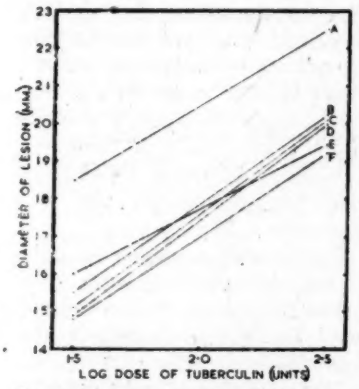
Cortisone has no direct effect on tuberculin allergy; its desensitizing action depends on dietary factors (Long, Miles,

TABLE I.—*Comparison of the Effect in Individual Treatment Groups with that in the Control Group (Same Experiment as Illustrated in Chart)*

Treatment	Potency Ratio*	Variance Ratio†	P
Pelleted diet+ D2a	0·23‡	20·28	<0·001
Cabbage and D2a	0·22§	17·42	<0·001
Ascorbic acid and D2a	0·24§	20·02	<0·001
Cabbage and propylthiouracil and D2a	0·14‡	41·99	<0·001
Cabbage and cortisone	0·18	22·49	<0·001

* Ratio of dose of tuberculin required to produce a reaction of given diameter in the controls (fed on pellets+cabbage), to corresponding dose in the treatment group.
† Ratio of "between treatments" variance to error variance.
‡ When cortisone was used instead of D2a the effect was not significant.
§ When cortisone was used instead of D2a the effect was significant.

and Perry, 1951a). It does not desensitize in guinea-pigs fed upon an ascorbic-acid-deficient diet, or on a diet supplemented with synthetic ascorbic acid, but only in animals provided with ascorbic acid in raw cabbage. Repetition of these experiments with D2a (10 mg. subcutaneously two hours before tuberculin), instead of cortisone (2 mg.), in B.C.G.-sensitized animals showed that the desensitizing action of the detergent, unlike that of cortisone, was independent of all these factors (see Table I and Chart). Furthermore, the desensitizing action of cortisone in cabbage-fed guinea-pigs is prevented by propylthiouracil and restored by minimal doses of thyroxine (Long, Miles, and Perry, 1951b). On the other hand, propylthiouracil administered under similar conditions did not influence desensitization by D2a (see Table I and Chart). The effect of D2a on tuberculin allergy may therefore be more direct than that of cortisone, since its action is linked neither with ascorbic acid metabolism nor with the activity of the thyroid.



Dose response to 32 and 320 i.u. tuberculin in sensitive guinea-pigs. A=controls; B=ascorbic acid+D2a; C=D2a; D=cabbage+D2a; E=cabbage+cortisone; F=cabbage+propylthiouracil+D2a.

Effect on Tuberculin Sensitivity and Antitoxic Immunity in the Same Animal

Three groups, each of ten guinea-pigs, were immunized by the subcutaneous injection into the left leg of 5 LF of diphtheria toxoid in 1 ml. normal saline; at the same time they were sensitized by the intramuscular injection into the right leg of 1.5 mg., dry weight, heat-killed virulent tubercle bacilli in 0.5 ml. liquid paraffin. Twenty-one days later the animals were immunized with a second dose of 5 LF diphtheria toxoid into the left leg. On the 23rd day one group was injected with 10 mg. of cortisone, a second with 50 mg. of D2a, while the third group, serving as controls, received 1 ml. normal saline alone; all injections were subcutaneous. The injections were repeated daily until the 31st day, when both flanks of the animals were depilated, and intracutaneous sensitivity to tuberculin estimated on the left side and to diphtheria toxin on the right side (Miles, 1949; Long, 1950). Both cortisone and D2a produced a comparable depression of tuberculin sensitivity, whereas neither influenced significantly skin sensitivity to diphtheria toxin in these immunized animals (see Table II).

TABLE II.—*Comparison of the Effect in Individual Treatment Groups with that in the Control Group*

Skin Response	Treatment	Potency Ratio*	Variance Ratio*	P
Bacterial allergy	Cortisone	0·33	23·19	<0·001
	D2a	0·46	18·39	<0·001
Antitoxic immunity	Cortisone	0·68	1·20	>0·2
	D2a	0·87	<1·0	—

* See Table I

All these animals were then bled by heart puncture, the serum was separated, and individual titrations of diphtheria antitoxin were carried out by the technique of Römer and Sames (1909). In addition, 1 ml. amounts of the sera of each of the three groups were pooled, and the antitoxin contents of the groups compared by passively immunizing guinea-pigs and testing their skin sensitivity to toxin, as described by Miles (1949). By neither method was it possible to detect differences in the antitoxin titre of the three groups. Thus it appears that under the conditions of this experiment neither cortisone nor D2a, in the heavy dosage employed, depressed antitoxin levels, nor did either prevent neutralization of intracutaneously injected toxin; nevertheless, both depressed tuberculin sensitivity to a similar degree, as previously observed.

Discussion

The present series of polyoxyethylene ethers represents a new type of antituberculous agent, with surface-active properties. Their mechanism is obscure, for, apart from producing submerged dispersed growth, they appear to have no direct action on the tubercle bacillus in the test-tube, even at 1% concentration, while there is no evidence of any antibacterial derivative in the blood taken from animals given large doses. Moreover, phagocytosis of tubercle bacilli is not increased, either *in vivo* or *in vitro*, by these agents (Rees and Hart, 1952).

The present work, by demonstrating a depression of skin sensitivity to tuberculin in the guinea-pig, shows that these surface-active agents have an effect on the host. This observation naturally invites comparison with other tuberculin-desensitizing substances, the most notable of which is cortisone (Long and Miles, 1950). The desensitizing effect of the present detergents is comparable in degree to that of cortisone, and, like the latter, does not affect antitoxic immunity in the guinea-pig; but there the analogy ends. For, first, the mechanism of the present effect is different, since it is independent of the dietary and hormonal influences that control the response to cortisone (cf. Long *et al.*, 1951a, 1951b, 1951c). Secondly, the detergents under study are antituberculous, whereas cortisone aggravates tuberculosis in mice (Hart and Rees, 1950). It is less certain that this steroid does so in the guinea-pig, which in resistance to cortisone, ascorbic acid metabolism, and ease of sensitization to allergens is more closely analogous to man than are the mouse and such creatures (Long, 1952). Nevertheless, dramatic effects in cortisone-sensitive animals, such as the mouse, rat, and rabbit, may indicate the trend of less obvious effects in cortisone-resistant creatures such as the guinea-pig and man.

The important role of cellular immunity, and of mononuclears in particular, in resistance to tuberculosis (Lurie, 1939a, 1939b, 1942) is virtually undisputed. On the other hand, repeated attempts to link humoral immunity and resistance to tuberculosis have failed (see, for example, Wilson and Miles, 1946). Cortisone causes lymphopenia and lymphoid atrophy in sensitive creatures (Wells and Kendall, 1940). Such effects are slight and inconstant in the guinea-pig, but, nevertheless, it is possible that cortisone-induced mesenchymal depression grossly outweighs the benefits of desensitization in cortisone-sensitive creatures, and cancels them in resistant ones. Thus only in animals treated with these detergents might anti-allergic activity exist without depression of the local cellular defence mechanism. This interpretation must remain hypothetical until further studies elucidate the problem.

However, we cannot overlook the most interesting observation that, whereas the chemotherapeutically active representatives of the present detergent series desensitized under the

conditions of our experiments, the inactive representatives did not. This association suggests that the mechanism of the chemotherapeutic action and that of the depression of sensitivity may have some common factor. Nevertheless, it must be admitted that there is at present little evidence in favour of the closer relationship of cause and effect—i.e., that the antituberculous effect is in fact due to desensitization. For although the many previous attempts to desensitize tuberculous guinea-pigs have had to be made with tuberculin, the results, taken as a whole, suggest little, if any, advantage to the host. Moreover, the present surface-active agents are equally effective in mouse and guinea-pig tuberculosis, in spite of the very different levels of allergy in these two species. Thus a tuberculin skin reaction cannot be elicited in the tuberculous mouse; and, although this animal can manifest a systemic reaction when tuberculin is given intravenously, much larger doses are required than in the guinea-pig (Smith, 1928; Rees and Hart, 1952). The influence on experimental tuberculosis of a number of other substances that depress tuberculin sensitivity, such as N-acetylsphingosine (Fisher *et al.*, 1951), dehydroascorbic acid and alloxan (Long *et al.*, 1951c), will be investigated. If these anti-allergic substances should also prove antituberculous, the hypothesis of a causal connexion between desensitization and chemotherapeutic activity would be strengthened.

Summary

The development of experimental tuberculosis in guinea-pigs is markedly inhibited by injection of certain surface-active polyoxyethylene ethers. Using the response to intracutaneous tuberculin as a measure of allergic hypersensitivity in albino guinea-pigs infected with B.C.G., we find that:

(1) Single subcutaneous or intravenous injections of these drugs diminish sensitivity to a degree comparable to that of cortisone.

(2) The chemotherapeutically active representatives of the series diminish tuberculin sensitivity, whereas the inactive members fail to do so.

(3) Their mode of action differs from that of cortisone, since it is independent of dietary factors and of thyroid activity.

(4) Neither D2a, a chemotherapeutically active detergent, nor cortisone, in heavy continual dosage, depressed skin sensitivity to diphtheria toxin, or antitoxin levels, in guinea-pigs immunized with diphtheria toxoid (in this experiment the animals were sensitized with dead tubercle bacilli). Both drugs depressed tuberculin sensitivity.

(5) The possible mode of action of these surface-active agents is discussed.

We are indebted to Dr. Knud Tolderlund, of the State Serum Institute, Copenhagen, for the B.C.G.; to Dr. J. W. Cornforth and Mr. J. A. Stock for preparing the series of surface-active agents; and to Dr. W. L. M. Perry for the statistical analyses.

REFERENCES

Bruce, H. M., and Parkes, A. S. (1947). *J. Hyg., Camb.*, 45, 70.
Cornforth, J. W., Hart, P. D'Arcy, Rees, R. J. W., and Stock, J. A. (1951). *Nature, Lond.*, 168, 150.
Fisher, N., Harington, C. R., and Long, D. A. (1951). *Lancet*, 2, 522.
Hart, P. D'Arcy, and Rees, R. J. W. (1950). *Ibid.*, 2, 391.
Long, D. A. (1950). *Brit. J. exp. Path.*, 31, 183.
—— (1952). *Bull. schweiz. Akad. med. Wiss.*, 8, 194.
—— and Miles, A. A. (1950). *Lancet*, 1, 492.
—— —— and Perry, W. L. M. (1951a). *Ibid.*, 1, 1085.
—— —— —— (1951b). *Ibid.*, 1, 1392.
—— —— —— (1951c). *Ibid.*, 2, 902.
Lurie, M. B. (1939a). *J. exp. Med.*, 69, 579.
—— (1939b). *Cyclopedia of Medicine, Surgery and Specialities*, p. 480. Davis, Philadelphia.
—— (1942). *J. exp. Med.*, 75, 247.
Miles, A. A. (1949). *Brit. J. exp. Path.*, 30, 319.
Rees, R. J. W., and Hart, P. D'Arcy (1952). Unpublished.
Römer, P. H., and Sames, Th. (1909). *Z. ImmunForsch.*, 3, 344.
Smith, M. I. (1928). *Publ. Hlth Rep., Wash.*, 43, 2817.
Wells, B. B., and Kendall, E. C. (1940). *Proc. Mayo Clin.*, 15, 133.
Wilson, G. S., and Miles, A. A. (1946). Topley and Wilson's *Principles of Bacteriology and Immunology*. Arnold, London.

TUBERCULOSIS IN FAMILIES WITH B.C.G.-VACCINATED AND NON-VACCINATED CHILDREN*

BY

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Since the introduction of B.C.G. vaccination 25 years ago much has been written to prove or disprove its value. In the Scandinavian countries, in particular, investigators gradually became convinced that the Calmette-Guérin vaccine had a very important part to play in the prevention of primary tuberculosis in both children and adults.

Many workers all over the world have reported surveys demonstrating the protective value of the vaccine. Others found little evidence to support this view. The problem of carrying out controlled investigations to cover all possible variables has made it very difficult to assess its true value. The report of an outbreak of tuberculosis in a school in Denmark in 1943, investigated by Hyge (1947), fulfilled many of the conditions necessary for a true analysis of the protective value of B.C.G. vaccination. The reports of Heimbeck (1929, 1932), Rosenthal, Blahd, and Leslie (1945), and Aronson (1948) are examples of investigations with different types of control groups.

Another approach to the problem is to examine those families in whom some children have been vaccinated and others not. The number of reports of such families in the literature are few. In France, Bertoye (1936) described a family of four children. The second child was vaccinated at birth because it was customary to vaccinate all infants at the maternity hospital where the child was born. In June, 1935, a domestic servant had an unexpected haemoptysis. She was immediately removed to hospital and the diagnosis of tuberculosis confirmed. The following month the three non-vaccinated children (aged 8, 5, and 1½ years) each developed a fever with hilar adenitis and a positive tuberculin reaction. The youngest child later died of tuberculous meningitis. The vaccinated child (aged 6 years) remained quite well.

Selection of Families

A search was made in the records of the Norrtull's Hospital, the Samariten Hospital, and the Central Tuberculosis Dispensary, Stockholm, for families satisfying all the following conditions:

1. That some children in the family had been vaccinated with B.C.G. and some not.

2. That every child said to have been B.C.G.-vaccinated was actually vaccinated and had been negative to 1 mg. of old tuberculin at the time of vaccination. (All B.C.G. vaccinations and the post-vaccinal tests are notified to the Central Tuberculosis Dispensary, and the records were consulted.)

3. That the tuberculin reaction was positive at the time of the check test (at about three months in infants and six weeks in older children).

4. That the tuberculin test had become positive following the vaccination before the time of exposure to an active case of adult tuberculosis.

*This work was carried out at the Paediatric Clinic of the Karolinska Institute, Norrtull's Hospital, Stockholm, during the period of tenure of a Cow and Gate Travelling Scholarship from the Department of Child Health, Queen's University, Belfast.

5. That all the children in the family (and, in this series, in all the families) had been vaccinated with vaccine made in the one laboratory—the Bacteriological Laboratory in Gothenburg.

6. That there was a definite confirmed case of active tuberculosis as the source of infection.

7. That all the children in the family had been in contact with the source of infection.

8. That the duration and time of contact with that case of tuberculosis (the source of infection) was the same for all the children.

In general, it may be stated that all families with B.C.G.-vaccinated and non-vaccinated children exposed to a known source of infection, and irrespective of whether or not there was any case of tuberculosis among the children, are included.

Family 1 (4 Children, 2 Adults)

One of twins, a girl aged 2 years, developed erythema nodosum in July, 1946. She was found to have *x*-ray evidence of primary tuberculosis, and a tuberculin-jelly test was positive. She was known to have been tuberculin-negative in February, 1946. She had not been vaccinated with B.C.G. When the family was called for a check-up it was found that the other twin, a boy, had an active hilar adenitis and was tuberculin-positive. He also had never been B.C.G.-vaccinated, but was known to have been tuberculin-negative in November, 1945.

The other two children had been B.C.G.-vaccinated—the 17-year-old girl in April, 1944, and the 16-year-old girl a year later. When examined on September 2, 1946, both had normal chest *x*-ray films and were Mantoux-positive. Repeat examinations in September, 1947, and September, 1948, showed normal chest *x*-ray films and positive Mantoux reactions.

In August, 1946, the mother was Mantoux-positive and had a normal chest *x*-ray film. Repeat yearly chest *x*-ray films up to 1951 remained normal. (She was also known to have had a normal chest *x*-ray film in March, 1934.) In August, 1946, the father was found to have active tuberculosis, with a positive sputum.

Family 2 (3 Children, 2 Adults)

The mother was discovered to have active tuberculosis with a positive sputum in April, 1949. On follow-up the same month the father's chest *x*-ray film was clear.

The three children were examined early in May, 1949. One, a 7-year-old girl who had not previously been B.C.G.-vaccinated, was discovered to have active primary tuberculosis with a positive tuberculin-jelly reaction. No previous tuberculin tests were known. At the time of examination she was found to have a pyrexia, which lasted two weeks. This was considered to be the initial fever.

The other two children had been B.C.G.-vaccinated—the 8-year-old boy in November, 1948, and the other boy, aged 10, the previous year. Both had normal chest *x*-ray films and were positive to tuberculin-jelly tests.

Family 3 (4 Children, 2 Adults)

The mother of this family had pleurisy in 1942 and developed lupus vulgaris in November, 1946. At this time her chest *x*-ray film showed nothing very definite—there was just a suspicion of a slight interlobar effusion. A year later her chest *x*-ray film was normal. However, in May, 1948, she was found to have pulmonary tuberculosis. On follow-up the same month (May, 1948) the father's *x*-ray film was normal, but a 14-year-old boy was found to have a raised temperature (considered the initial fever), persisting for some weeks. His *x*-ray film showed primary tuberculosis and his Mantoux reaction was positive. There was no knowledge of previous tuberculin tests and he had not been B.C.G.-vaccinated.

Two boys, aged 4 and 5 years, were B.C.G.-vaccinated in 1944 and 1943 respectively. The 15-year-old girl had been B.C.G.-vaccinated in 1941. These three children had normal chest *x*-ray films and were positive to tuberculin tests in May, 1948.

Family 4 (3 Children, 2 Adults)

A 4-year-old boy was found to be positive to the tuberculin-jelly test and to have a hilar adenitis in October, 1948. His E.S.R. was 34 mm. in one hour. The previous June he was known to have had a rise in temperature lasting about three weeks. This may have been the initial fever. There was no knowledge of previous tuberculin tests and he had never been B.C.G.-vaccinated.

At a follow-up examination in November, 1948, a second boy, aged 6 years, was found to have primary tuberculosis. His tuberculin-jelly reaction was positive and his E.S.R. 41 mm. in one hour. Tubercle bacilli were isolated from his gastric washings. This boy also had a history of a rise in temperature in June, 1948. Again there were no known tuberculin tests, and he had not been B.C.G.-vaccinated.

The third child, a boy aged 14, had been vaccinated with B.C.G. in November, 1945. On follow-up examination in December, 1948, he was positive to tuberculin jelly and his chest *x*-ray film was normal.

The parents were examined in December, 1948. The father's chest *x*-ray film showed active tuberculosis. He also gave a history of an attack of pneumonia the previous May. At this time the mother's *x*-ray film showed some suspicious changes, and these progressed to obvious active disease within a year. Her Mantoux reaction was positive.

Family 5 (2 Children, 2 Adults)

A 2-year-old boy was negative to the tuberculin-jelly test in May, 1946. In June, 1946, this test was strongly positive, and he was found to have an active hilar adenitis. He ran a high temperature—the initial fever—for a fortnight. He had not been B.C.G.-vaccinated.

At a follow-up examination in June, 1946, his 5-year-old brother, who had been vaccinated with B.C.G. in the autumn of 1945, had a positive tuberculin-jelly reaction and a normal chest *x*-ray film.

The mother was examined the same month. She was tuberculin-positive and an *x*-ray film of her chest was normal. Yearly repeat examinations for the next four years were clear. The father was examined in July, 1946. His chest *x*-ray film showed active tuberculosis and his sputum contained tubercle bacilli.

Family 6 (4 Children, 2 Adults)

On Christmas Eve, 1947, three of the children (girls aged 3, 4, and 6 years) developed erythema nodosum. All were positive to tuberculin-jelly tests and suffering from primary tuberculosis. There were no known previous tuberculin tests, and none of them had been vaccinated with B.C.G.

At a follow-up examination the 2-year-old girl, who had been B.C.G.-vaccinated shortly after birth in November, 1945, was found to have some suspicious enlargement of the hilar glands and to be tuberculin-positive. She had a history of having just recovered from whooping-cough. Her hilar shadows were considered to be within normal limits in three months and again a year later.

The follow-up examination showed that chest *x*-ray films of both parents were normal. It was then found that an uncle had arrived on November 21, 1947, and stayed with them for three weeks; during this time he had become ill. He was admitted to a sanatorium on January 4, 1948, with cavitation and a positive sputum.

Family 7 (3 Children, 2 Adults)

A boy aged 4 years was first seen in October, 1949, and there was a history of his "not being well" since the previous July, when he was known to have had a rise in temperature for some weeks. He was found to be positive to tuberculin jelly and had a primary complex. On looking

back it was thought that his initial fever may have occurred in July. He had never been vaccinated with B.C.G. and he was not known to have had any previous tuberculin tests.

At a follow-up examination in October, 1949, the 11-year-old boy was also found to have a positive tuberculin reaction. At first his chest *x*-ray film was suspicious. His E.S.R. was 7 mm. in one hour. Further *x*-ray films did not show any change and there was little evidence of active disease at any time. He had not been B.C.G.-vaccinated and he was not known to have had any previous tuberculin tests.

The 8-year-old girl, who had been vaccinated with B.C.G. the previous year, had a normal chest *x*-ray film and was Mantoux-positive (1 mg.).

Both parents were examined in October, 1949. Their chest *x*-ray films were normal and both were positive to 0.05 mg. of old tuberculin.

It was then found that the three children had been staying with their grandmother during the summer. She was examined in the local tuberculosis clinic in October, 1949, and evidence of old changes was found on the chest *x*-ray film. During this investigation a suspicion arose that a friend of the family with whom the children had been in contact might be the source. He was called for examination and was found to be Mantoux-positive (0.05 mg.). His chest *x*-ray film showed active tuberculosis, and tubercle bacilli were isolated from his sputum during the first week of November, 1949.

Family 8 (2 Children, 2 Adults)

The mother's sister was found to have tuberculosis in 1947. Tubercle bacilli were present in her sputum, and she died two years later. She was known to have had a chest lesion in 1941.

At a follow-up examination in April, 1947, the 6-year-old boy was found to be positive to the tuberculin-jelly test and to show radiological evidence of primary tuberculosis. Besides the recent contact with his aunt, he had lived with her for a period in 1943. However, his chest *x*-ray films were normal in October, 1945, and June, 1946. He had not been vaccinated with B.C.G.

His 5-year-old sister was B.C.G.-vaccinated in 1941. There is some doubt about the post-vaccinal tuberculin test. The case records showed her to have been positive then, but the mother could not recall it. She was now tuberculin-positive. She had normal *x*-ray films between January, 1945, and April, 1947. In November, 1947, there was some degree of hilar enlargement, but an *x*-ray film six weeks later was normal. Her E.S.R. in April and December, 1947, was 5 mm. in one hour, and in March, 1948, 10 mm. in one hour.

A third child*, a boy, was born in September, 1946, and vaccinated with B.C.G. a short time after birth. He was kept in a children's home for his first year of life and never had any contact with his tuberculous aunt. Six *x*-ray films between November, 1947, and January, 1951, were normal. Yearly tuberculin tests up to January, 1951, remained positive.

The parents' *x*-ray films did not show any evidence of tuberculosis, but the mother did have a lesion in 1942. She never had any tubercle bacilli in her sputum.

Family 9 (2 Children, 2 Adults)

The father of this family was found to have active tuberculosis in November, 1948, and a positive sputum. His Mantoux reaction (0.05 mg.) was positive. His wife had been B.C.G.-vaccinated in November, 1947. On follow-up she was still Mantoux-positive (0.05 mg.) and had a normal chest *x*-ray film.

*This child is excluded from the investigation as he had no contact with the source of infection. The other two children had three possible times of infection—from the aunt in 1941, their mother in 1942, and again their aunt in 1947. In view of the *x*-ray findings it seems likely that these children were infected just before the aunt was discovered, in April, 1947, to have become active again.

The 2-year-old girl was examined in the first week of January, 1949. She was positive to the tuberculin-jelly test and had an active hilar adenitis. A few weeks later her E.S.R. was 40 mm. in one hour. There was also a history of a rise in temperature just before Christmas, 1948, and it was thought possible that this may have been the initial fever. She had not been vaccinated with B.C.G., and there were no known previous tuberculin tests.

An 11-months-old boy had been B.C.G.-vaccinated at birth. His chest *x*-ray film was normal and a tuberculin-jelly test was positive.

Family 10 (2 Children, 2 Adults)

An uncle of these children was known to have had tuberculosis in 1944 and to be Mantoux-positive. The two children were in contact with him off and on from the spring of 1946 to the beginning of 1947. He was then discovered to have tubercle bacilli in his sputum.

At a follow-up examination in March, 1947, the 4½-year-old girl was positive to the tuberculin-jelly test and had active primary tuberculosis. She had not been vaccinated with B.C.G., but was known to have been tuberculin-negative three months before.

The 15-year-old boy had been B.C.G.-vaccinated in 1944. His Mantoux (0.05 mg.) was positive and his chest *x*-ray film normal.

Both parents, when examined in March, 1947, were Mantoux-positive (0.05 mg.) and their chest *x*-ray films normal.

Family 11 (4 Children, 2 Adults)

A 4-year-old girl was found to be positive to the tuberculin-jelly test in the second week of January, 1950, and to have primary tuberculosis. No previous tuberculin tests were known, and she had not been B.C.G.-vaccinated.

At a follow-up examination the same month the 7-year-old boy was found to be positive to the tuberculin-jelly test and to have active hilar adenitis. It was considered that a rise in temperature he had had in December, 1949, may have been the initial fever. There were no known previous tuberculin tests and he had not been vaccinated with B.C.G.

The 1-year-old boy had been B.C.G.-vaccinated at birth and the 11-year-old boy over two years previously. Both were tuberculin-positive and had normal chest *x*-ray films.

When the father was examined he was found to have evidence of active tuberculosis. There was no record of the mother having been *x*-rayed.

Family 12 (2 Children, 2 Adults)

After the discovery of active pulmonary tuberculosis in their aunt this family was investigated in October, 1944. This aunt had also had tuberculosis of a foot bone and erythema nodosum twice. No tubercle bacilli had ever been found in her sputum.

The 3-year-old boy was tuberculin-positive and had an active hilar adenitis. There was no knowledge of previous tuberculin tests and he had not been B.C.G.-vaccinated.

The 9-months-old boy had been B.C.G.-vaccinated at birth. His chest *x*-ray film was normal and he was tuberculin-positive.

The mother's chest *x*-ray film was clear and she was Mantoux-positive (1 mg.). The father was never traced, as he had deserted the family.

Family 13 (2 Children, 2 Adults)

The 3-year-old boy developed phlyctenular conjunctivitis in October, 1947. He was Mantoux-positive (0.05 mg.) and had active hilar adenitis. There were no known previous tuberculin tests and he had not been vaccinated with B.C.G.

At a follow-up examination in November, 1947, the 2-year-old boy, who had been B.C.G.-vaccinated at birth, was found to be positive to the tuberculin-jelly test and to have a normal chest *x*-ray film.

The parents were also examined in November, 1947. The mother was Mantoux-positive (0.05 mg.) and had a clear chest *x*-ray film. The father was also Mantoux-positive (0.05 mg.), but he had a positive sputum, and a tuberculous cavity was shown on the chest *x*-ray film.

Family 14 (2 Children, 2 Adults)

A 1½-year-old boy was admitted to hospital with erythema nodosum at the end of October, 1945. His tuberculin-jelly test was positive and he had an active primary tuberculosis. There were no known previous tuberculin tests and he had not been vaccinated with B.C.G.

The 4-year-old boy had been B.C.G.-vaccinated in November, 1942. In November, 1945, he was tuberculin-positive and his chest *x*-ray film was clear.

Both parents were Mantoux-positive and had clear *x*-ray films. An aunt with whom the children had been in contact was now suspected. She had a positive sputum, and multiple cavities were shown on an *x*-ray film. She died seven months later.

Family 15 (2 Children, 2 Adults)

A 2½-year-old boy was found on routine examination to be positive to a tuberculin-jelly test in April, 1948, and to have a hilar adenitis. There were no known previous tuberculin tests and he had not been vaccinated with B.C.G.

The 4½-year-old boy had been B.C.G.-vaccinated in April, 1946. His tuberculin-jelly test was positive and his chest *x*-ray film clear on follow-up examination in April, 1948.

The mother's chest *x*-ray film was clear and she was Mantoux-positive (0.05 mg.). The father was known to have had tuberculosis in 1940. He was examined twice yearly from then on, but was never regarded as infectious. He was at work all this time. Their maid, who was found to have active bilateral tuberculosis towards the end of 1947, was considered the source of infection.

Family 16 (3 Children, 2 Adults)

A 6-year-old boy developed chicken-pox in 1948. He did not quite recover, but remained "out of sorts." During the first few days of January, 1949, he was found to be tuberculin-positive and to have primary tuberculosis. There was no knowledge of previous tuberculin tests and he had not been vaccinated with B.C.G.

Twin girls aged 1½ years had been B.C.G.-vaccinated in July, 1947. They were both tuberculin-positive (jelly and 0.05 mg. old tuberculin) and both had normal chest *x*-ray films.

Both parents were also Mantoux-positive (0.05 mg.) in January, 1945, and their chest *x*-ray films were clear.

It was then discovered that the family had visited their grandfather between October and Christmas, 1948. (Their grandmother had died 25 years previously with tuberculosis.) The grandfather was examined in February, 1949. He was found to be tuberculin-positive and to have active tuberculosis.

Comment on Cases

The diagnosis of primary tuberculosis was confirmed by the head of each hospital. (Families 1–10 by Professor A. Wallgren at Norrtull's Hospital and families 13–16 by Professor N. M. Malmberg at the Samariten Hospital. In family 11, one child was admitted to Norrtull's and the other to the Samariten. Family 12 was seen only at the Central Tuberculosis Dispensary.) All the children not admitted to hospital, the parents, and other relatives, etc., were examined by tuberculosis medical officers in the Central Dispensary, except those, sometimes the sources of infection, living in country districts, who were examined by local tuberculosis officers and admitted to local sanatoria.

Tubercle bacilli were isolated from the gastric washings of some of the children with primary tuberculosis, but no gastric washings were carried out in the vaccinated children. Hence this part of the investigation is of no value.

Discussion

In all there were 16 families, with 22 vaccinated and 22 non-vaccinated children, and each family satisfied all the given conditions. There is therefore a group of children some of whom act as controls and the others as tests of the protective value of their B.C.G. vaccination. The source of infection for all the children, while not the same, is at least similar. Within each family the familial susceptibility to tuberculosis is probably the same, although the resistance may be influenced by the age composition of the family.

When the source of infection lies in the home, it may be assumed that each child was exposed to the maximum possible risk. The social conditions, especially overcrowding, will vary between each family, but the children in each individual family will live under the same conditions and their standard of nutrition will tend to be the same.

Why some children should have been vaccinated and others not is not very clear. It seems most likely that the mother was offered vaccination for some of the children on one particular occasion—for example, at a school medical examination, at a child welfare centre, or at a maternity hospital—but did not trouble to have the remaining children vaccinated.

One criticism might be that the non-vaccinated children were left because they were known to be tuberculin-positive. In most of the non-vaccinated children there were no known previous tuberculin tests. This, coupled with the presence of active primary disease, would make it unlikely that they had been tuberculin-positive when the other children were vaccinated with B.C.G. One possible exception might be the boy aged 11 in family 7.

There is no reason to believe that any form of selection (such as not vaccinating a child with a chronic illness) occurred among either group of children. It is often said that only the most careful and intelligent mothers will have their children vaccinated, and that this in itself is a great source of selection when using non-vaccinated children in other families as controls. This does not apply to the present series.

The question of race does not arise so far as comparison between each group is concerned, as all the children were Swedish. The possibility of an occupational risk has to be considered in the older children. All the non-vaccinated were 14 years or under (20 of the 22 were under 9 years). There can be no question of an occupational risk in this group. Four of the vaccinated children were 15 years or over; three of them were girls. Despite the known increased risk at puberty and during adolescence, especially in females, and despite a known intimate contact with a source of infection, all these four children (and a 14-year-old boy) were completely protected. Indeed, it must be expected that these older children will have a greater circle of acquaintances outside the immediate family circle and will have the added risk of a casual infection.

It is very unlikely that the question of sex is important before puberty. Age, however, is most important. It is generally accepted that children under 5 years have a much more severe reaction to a primary tuberculous infection than older children. Two of the B.C.G.-vaccinated children had suspicious *x*-ray films at first (families 6 and 8). Both were under 5 years old, and were the youngest in the family. This probably occurred by chance, because suspicious lesions may occur in B.C.G.-vaccinated children at any age. It is worth noting that the mother of family 6 volunteered the information that, of all her children, the youngest (aged 2) had played continuously with the source of infection for days before his tuberculosis was suspected. In neither of the cases did definite primary tuberculosis develop. On the other hand, a non-vaccinated boy aged 11 (family 7) was under suspicion at first, while his younger brother, aged 4, had a typical infection and his sister, aged 8, who was vaccinated with B.C.G., was completely protected.

Table I shows the classification of the children into four age groups, according to whether they were B.C.G.-vaccinated or not. It is seen that, in general, the vaccinated children

TABLE I

Age	Non-vaccinated			Vaccinated		
	Obvious Primary Tuberculous Complex	Suspect Primary Tuberculous Complex	Total	No Evidence of Primary Tuberculous Complex	Suspect Primary Tuberculous Complex	Total
0– ..	14	0	14	9	1	10
5– ..	6	0	6	4	1	5
10– ..	1	1	2	3	0	3
15+ ..	0	0	0	4	0	4
	21	1	22	20	2	22

were in the minority in the two lowest groups and in the majority in the highest. This is of importance, as it is likely that the young children were more at home than the older children and therefore more exposed to any source of infection within the family. It is of interest, however, to look separately at the different age groups. One child among the vaccinated in each of the two lower age groups had some clinical evidence of primary infection—that is, one of the 10 B.C.G.-vaccinated children under the age of 5 years had some evidence of primary infection, whereas all 14 of the non-vaccinated became clinically ill. Similarly, only one of the five vaccinated children between 5 and 10 years developed some evidence of primary disease, compared with obvious infection in the six non-vaccinated. The other two groups are too small for any conclusions to be drawn.

Family 1 contains two adolescent girls protected, and twins aged 2 years who developed erythema nodosum and primary tuberculosis. In family 16, twins aged 1½ years were protected and a boy of 6 years was infected. Family 3 shows a 14-year-old boy infected and a girl of 15 years and two boys aged 4 and 5 years protected. Families 9 and 12 have two children under 1 year protected, while the other children were infected. In family 11, the two protected children were aged 1 year and 11 years and the two infected children were in between (aged 4 and 7 years). Even in such a small group, then, there is evidence of protection at all ages of childhood. No cases of tuberculous meningitis or miliary tuberculosis occurred in either group.

Table II shows the distribution of the children, by families, in each group and the source of infection. In 8 of the 16 families the source was either the father or the mother; in 5 an aunt or an uncle; and in the rest a grandfather, a maid, and a friend of relatives whom that family had visited. The mother of family 8 had had tuberculosis five years before, but was not considered likely to be infectious at the time. The children had, however, been in contact with an aunt who was found to have active tuberculosis and who died two years later.

TABLE II.—*Distribution of the Children in Each Group According to Families with Source of Infection*

Family	Non-vaccinated Primary Tuberculosis	B.C.G. vaccinated Tuberculin-positive but no Evidence of Active Tuberculous Infection	Source of Infection
1	2	2	Father
2	1	2	Mother
3	1	3	"
4	2	1	Father
5	1	1	"
6	3	1†	Uncle
7	2*	1	Friend of relatives
8	1	1†	Aunt
9	1	1	Father
10	1	1	Uncle
11	2	2	Father
12	1	1	Aunt
13	1	1	Father
14	1	1	Aunt
15	1	1	Maid
16	1	2	Grandfather

* One boy with no definite clinical disease.
† Each child had a suspicious *x*-ray film at first.

B.C.G. vaccination offers a relative rather than a complete protection against primary tuberculosis—that is, it raises the resistance to a subsequent superinfection with virulent organisms. It is most likely that all the vaccinated children in this series were superinfected, but only two showed a possible hilar reaction of short duration.

The incidence of tuberculosis in vaccinated and non-vaccinated children admitted to Norrtull's Hospital between 1945 and 1949 inclusive is interesting. Of 625 cases of primary tuberculosis, 26 had been vaccinated with B.C.G. (excluding 9 who had been vaccinated during the incubation period); 12 of these 26 cases were mild and 14 more or less typical, but some of the latter had been vaccinated so long before that it is very likely the immunity had disappeared. In addition, there were 137 cases with spontaneous positive tuberculin reactions. During this five-year period 1,352 vaccinated children were admitted and 7,279 non-vaccinated; and 26 (1.9%) of the vaccinated children had tuberculosis, compared with 599 (8.2%) cases among the non-vaccinated children. There were 28 cases of tuberculous meningitis and/or miliary tuberculosis in the non-vaccinated group and none in the vaccinated group. These figures are not representative of the children of Stockholm, and apply only to the hospital admissions.

The difference in the number of vaccinated and non-vaccinated is surprisingly great. This is partly explained by the fact that in the non-vaccinated group are included infants under 3 months who were vaccinated at birth but were not yet tuberculin-positive, and partly because there has been a very great increase in the number of vaccinations in recent years, so that the proportions for 1949 are quite different from those of 1945. Parallel with this rise in the number of vaccinated children there has been a fall in the number of cases of primary tuberculosis—from 183 admissions in 1945 to 88 in 1949, with an average of 123 in the intervening years.

Summary

A description is given of 16 families in which some children were vaccinated with B.C.G. and others not, and in which all had been exposed to a known source of infection. Reasons are put forward for considering the two groups comparable. Among the 22 children in the non-vaccinated group 21 developed primary tuberculosis. In the B.C.G.-vaccinated group, two at most showed some evidence of superinfection.

The protective value of B.C.G. vaccination is striking, both when the source of infection is within the family (with the maximum risk for each child) and when it is outside.

The difference in the incidence of tuberculosis in the vaccinated and non-vaccinated children admitted to Norrtull's Hospital is recorded and a brief description of the fall in the number of cases of primary tuberculosis from 1945 on is given. The absence of tuberculous meningitis and miliary tuberculosis in the vaccinated group is noted.

I wish to thank Professor N. M. Malmberg and Dr. C. M. A. Gentz for granting me access to the records of the Samariten Hospital and the Central Tuberculosis Dispensary respectively, and to express my appreciation to Dr. Sven-Ivar Rollof for his help in the interpretation of the case records. I should especially like to thank Professor A. Wallgren for his constant help, encouragement, and criticism in the preparation of this paper.

REFERENCES

Aronson, J. D. (1948). *Amer. Rev. Tuberc.*, **58**, 255.
Bertoye, M. P. (1936). *Lyon méd.*, **157**, 77.
Heimbeck, J. (1929). *Ann. Inst. Pasteur*, **43**, 1229.
—— (1932). *Arch. intern. Med.*, **49**, 957.
Hyge, T. V. (1947). *Acta tuberc. scand.*, **21**, 1.
Rosenthal, S. R., Blahd, M., and Leslie, E. I. (1945). *J. Pediat.*, **26**, 470.

HEAD-DROPPING TEST

BY

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This test serves, first of all, in the early diagnosis of paralysis agitans and post-encephalitic Parkinsonism. The latter term is an awkward one, and has already led to such a stylistic horror as "Rombergism," to which "Babinskiism," it is hoped, will not be added. Therefore the generic term "Parkinson's syndrome" is used here, and the terms "idiopathic," "post-encephalitic," etc., are used to distinguish the varieties.

It is easy to diagnose a fully developed case of Parkinson's syndrome of any variety. Often there is an immediate impression of the condition which later proves to be correct, although at the time the impression was gained no adequate proof could be offered. However, it is sometimes difficult to diagnose cases that are just beginning to manifest themselves, or abortive cases, the so-called "formes frustes." The beginning and the course of Parkinson's syndrome of any variety is usually insidious and slow, and this makes the diagnosis particularly difficult.

In post-encephalitic Parkinson's syndrome it may be impossible to obtain a clear history of encephalitis, or the encephalitis may have occurred as long as 15 or 20 years previously, rendering some histories unreliable. The long so-called pseudo-neurasthenic stage of post-encephalitic Parkinson's syndrome, with its manifold and vague symptoms, particularly contributes to the diagnostic confusion. Many and varied morbid conditions must be considered in the differential diagnosis in such cases: diverse degenerative and non-degenerative diseases of the brain, multiple sclerosis, exophthalmic goitre, senile tremor, familial tremor, arthritis, as well as psychoneurotic, neurasthenic, and hysteric states and various intoxications.

How difficult to some clinicians the diagnosis may be is drastically demonstrated by the fact that I have seen patients with unmistakable Parkinson's syndrome who previously had been subjected to encephalography and angiography in the search for a tumour.

Tests in Early Diagnosis of Parkinson's Syndrome

The early diagnosis of this condition has long engrossed investigators, and many tests have been devised for this purpose. Some of these are: (1) Abnormal position of hand and fingers, particularly of the thumb. (2) Easy exhaustibility of fine finger movements. (3) Positive push test: on a sudden push backward, the patient, standing erect, does not involuntarily dorsiflex the foot and toes on the affected side. (4) Arm-deviation test: When the patient, with his eyes closed, stands with arms outstretched in front of him there is a tendency for the arms to move inward and downward. (5) Overestimation of weight of objects placed in the affected hand. (6) Cogwheel rigidity of muscles: On quick passive stretching, the examiner feels short jerks in the stretched muscles of the patient. (7) Fixation of position test (a so-called postural reflex): The examiner places his thumb on the biceps tendon, and with the other hand passively flexes the forearm of the patient; on every movement the thumb feels that the biceps tendon tightens so as to fixate the forearm in every given position. (8) Paresis of convergence of the eye muscles. (9) Hypometria, micrographia. All these tests have a sound physiological basis, and are useful. However, it cannot be said that they become manifest early in the disease.

For many years I have been accustomed to base the diagnosis of early Parkinson's syndrome on the following tests: (1) Exaggeration of the orbicularis oculi reflex: closure of the eyes on tapping the glabella (Wartenberg, 1945). (2) Diminution of pendulousness of the arms in walking, and diminution of pendulousness of the legs. For the latter test the patient sits on the table with his legs hanging freely. The examiner lifts the legs, lets them swing freely, and appraises their swinging time. This time is conspicuously shorter in Parkinson's syndrome, particularly when only one side is affected (Wartenberg, 1951). (3) Increased resistance in the neck muscles as felt by the examiner when he moves the head of the patient in different directions.

This third test, based on the rigidity of the neck muscles, has seemed particularly useful, though the method is somewhat crude. However, its physiological rationale is sound.

Tremor and Rigidity

The fundamental motor disturbances in Parkinson's syndrome can be traced to two main factors—tremor and rigidity. Which of these is the more important? The first observers stressed tremor. This is understandable, since, both for the patient and for the doctor, it is the more conspicuous, the more striking manifestation of the disease, especially so since the tremor affects predominantly the distal parts of the extremities, and is more obvious and disturbing to the patient. I have seen many such patients with both tremor and rigidity who complained only of the tremor.

Later investigators stressed rigidity at the expense of tremor. The tendency has now become to regard tremor as the non-essential, secondary feature, and to emphasize the existence of paralysis agitans *sine agitatione*. "I for my part," said Lewy (1932), "reject paralysis agitans *sine rigiditate*." This is in accordance with my own experience. I have seen patients with Parkinson's syndrome of any variety showing rigidity without tremor. For me the more significant element of the pallidal syndrome is rigidity, which is always present. Wilson (1940, p. 799), however, said: "Examples of paralysis agitans *sine rigiditate* are seen once in a while; they include akinesis, tremor, sometimes Parkinsonian postures, but not hypertonia." Though there is certainly Parkinson's syndrome without tremor, I doubt very much that there is Parkinson's syndrome without rigidity. In cases in which allegedly there was no rigidity the technique of examining for tonus has probably been faulty.

What comes first in the syndrome, tremor or rigidity? Many textbooks assert that in most cases tremor is the first sign. But it is admitted that occasionally tremor may appear some years after rigidity. Gowers (1893) found that rigidity may constitute "the first symptom of the disease." According to Wilson (1940, p. 791), "slowness and rigidity precede visible shaking in a considerable number." It is the post-encephalitic condition, particularly, that may show marked rigidity in the early stages, and only later may the tremor become apparent.

Where does rigidity in Parkinson's syndrome start? It is generally assumed that it starts in the proximal muscles of the limbs, particularly the upper. It is my belief that the rigidity starts in the neck and shoulder muscles, particularly in the flexors of the head. This leads to the sustained flexor position of the head, an early sign. As the disease advances and spreads this rigidity still remains more pronounced in the flexors of the head than in any other muscles of the body.

The textbooks point out the occurrence of the hemiparkinson syndrome. I would also like to stress the occurrence of a cervico-brachial type. This type is seen particularly in the idiopathic variety. In such cases the rigidity affects the muscles of the neck and shoulders predominantly or exclusively. The leg muscles are much less affected, or not affected at all.

Neck Rigidity

My long-held view that rigidity in Parkinson's syndrome affects the muscles of the neck first and foremost I found also to be held by Vujic (1927). He speaks of "pronounced extrapyramidal hypertonia of the neck muscles," in cases of post-encephalitic Parkinson's syndrome. "The same hypertonia," says Vujic, "is often found in the limbs in less pronounced degree, sometimes much more distinctly in the arms than in the legs, and especially in the proximal parts.... Hypertonia is ascertained by means of passive movement of the head and limbs."

In photographs of some cases the prominence and tension of the sternocleidomastoid muscles which produce the forward bending of the head are conspicuous. "In the recumbent posture sternomastoids do not slacken" (Wilson, 1940, p. 794). How strongly this position of forward bending of the head is can be demonstrated convincingly by the following. When a patient with advanced Parkinson's syndrome is asked to lie supine, his occiput does not touch the supporting surface on which he lies. He keeps his head up from the surface indefinitely, even if he is admonished to relax (see illustration).

Advanced Parkinson's syndrome. Typical posture of head of patient lying supine: the head is kept flexed indefinitely and off the surface.

Professor Robert Bing has drawn my attention to the fact that Steck (1926, 1927) apparently was the first to describe this *oreiller psychique* (psychic pillow), which was seen in his patients with psychosis accompanied by extrapyramidal syndromes. Steck graphically illustrated this "psychic pillow." While the phenomenon was found by him in psychotic patients who had extrapyramidal signs, none of my patients was in any way psychotic, and the "psychic pillow" was used here exclusively to the extrapyramidal rigidity of the neck muscles. The term "psychic pillow" certainly cannot be applied to cases of Parkinson's syndrome. The "pillow" here is not "psychic" but grossly "organic." It is hardly correct to call it "psychic" even in Steck's cases with psychosis, since these show extrapyramidal syndromes to which this position of the head must be attributed in the first place.

From a physiological standpoint this early bending position of the head in Parkinson's syndrome is easy to understand. The postural factor is considered to be determined by the "loss of righting reflex" (Brock and Wechsler, 1927), fundamental for this disease. In Parkinson's syndrome there is a "dissolution of erectness" (Kraus, 1924), a disintegration of the erect posture in man. The forward bending of the head is the very first expression of this disintegration.

If this be so, if indeed rigidity of the neck muscles is an early sign of Parkinson's syndrome, then the best test for this rigidity would be a test which demonstrates the rigidity of the flexors of the head. This, in fact, is the basis for the head-dropping test.

Technique of the Head-dropping Test

The patient lies supine on a horizontal examining table, without a pillow. The surface should not be hard, but padded. He is made to relax completely and should not try to raise his head, as he is always inclined to do. He is asked to close his eyes, his attention is diverted, and he is engaged in conversation. His head rests on the table surface. The examiner places his left hand under the patient's occiput, the dorsum resting on the table and the occiput lying in the examiner's palm. Then, with his right hand, the examiner suddenly, unexpectedly, and briskly lifts the patient's head and allows it to drop.

In normal persons the head drops back on to the left hand of the examiner with force, like a dead weight. It is as if there were no tonus of the neck muscles at all, as if the head were attached to the body by a string. This complete lack of tonus is in gross contradistinction to the marked tonus the neck muscles exhibit when the patient is erect. One is amazed at the sharp impact with which the head falls heavily and inertly backwards, an impact felt distinctly by the examiner. The fall is so heavy that, were it to occur on a hard surface, the patient could sustain an injury. It even might hurt him if his head should happen to fall on a ring the examiner was wearing. It is essential that the patient be completely relaxed. In the rare instances where complete relaxation cannot be achieved the test must be given up for the time being. In any case it is advisable to repeat the test. If after several examinations varying results are obtained the heaviest drop counts; in all others it must be assumed that some active interference has taken place on the part of the patient.

The test can also be performed on the patient lying prone, or on either side, but it is much more easily performed and its results are less difficult to evaluate when the patient lies supine. The rigidity of the neck muscles is evidently greater in the flexors than in the retractors of the head. It must be assumed, therefore, that the dropping of the head is slower when the patient lies supine than when he lies prone. However, this is difficult to prove.

The most striking change from the normal in this head-dropping test is seen in Parkinson's syndrome even in the earliest stages. Here the head drops slowly and gently; the downward movement is, so to speak, reluctant, hesitant, and lazy. The slow dropping of the head shows that, though the rigidity of the muscles in Parkinson's syndrome is generally diminished when the patient assumes a recumbent position, the rigidity of the neck muscles still remains considerable. In character this movement is the same as that felt by the examiner when he passively stretches a rigid extremity. The downward movement of the head maintains an even flow, is smooth, and is uniform from beginning to end. There is no sudden "give," no erratic unevenness. The smoothness and evenness of the movement are clearly seen in slow-motion pictures. If the patient interferes voluntarily and makes a movement with his head, this immediately can be distinguished as such.

The examiner is able to appraise the character of the motion not only by sight but by touch as well. In the palm of his hand he can feel the degree of impact of the dropping head. Compared with the violent impact in normal subjects, in Parkinson's syndrome the head drops softly and smoothly. The difference between the normal and the pathological is unmistakable, even in the earliest stages of the syndrome. I have seen quite a number of patients with Parkinson's syndrome who did not complain of rigidity anywhere, yet in whom the head-dropping test proved to be typical for this disease. In advanced cases the test is not necessary. Here the rigidity of the neck muscles is too obvious to need any special tests. As shown above, this rigidity is strikingly illustrated by the fact that the patient with advanced Parkinson's syndrome lying supine keeps his head bent and off the surface (see illustration). This is, so to speak, a "frozen" head-dropping test. In Parkinson's syndrome the test has

been found abnormal so regularly, and this abnormality has been so clear and unequivocal, that I dare state that if the head-dropping test is normal the syndrome can be excluded.

The Test in Differential Diagnosis

The test is of great importance in differential diagnosis: Parkinson's syndrome *versus* senile tremor.

I have seen cases of tremor diagnosed by authorities as Parkinson's syndrome in which the head-dropping test was later found to be normal. This led to further clinical investigation which proved beyond doubt that the patient suffered from senile tremor and not Parkinson's syndrome. Again and again I have found that the latter diagnosis is made too often. The differential diagnosis between these two conditions may be very difficult, since they have many clinical features in common. It is true that there is a difference between senile and parkinsonian tremor, yet tremor *per se* gives no decisive clue for differential diagnosis. The outstanding characteristic of senile tremor—involvement of the head—may occur also in Parkinson's syndrome. It is therefore understandable that many authors, even quite recently, have maintained that the senile tremor is just a "forme fruste" of paralysis agitans. However, a differential diagnosis is of importance particularly with regard to prognosis, since senile tremor is a benign, non-progressive lesion, while Parkinson's syndrome is not. In this differential diagnosis, parkinsonian tremor *versus* senile tremor, the head-dropping test is of decisive importance.

The outstanding sign of the senile tremor is the invariable absence of rigidity. The head-dropping test, being the most sensitive test for rigidity, decides the issue. It is always unmistakably and completely normal in senile tremor.

Dr. Charles Kunkle tried this test on a 70-year-old woman who had had a typical essential heredofamilial tremor for 30 years. In a personal communication he states: "When put to the test her head dropped in entirely normal fashion, like a true dead weight."

Other Tests

Next to the head-dropping test, the following have proved to be helpful in the early diagnosis of Parkinson's syndrome:

(*a*) *Shoulder-shaking Test.*—The examiner places his hands on the patient's shoulders, shakes them briskly by alternating movements to and fro, and observes the passive swinging of the arms thus produced. On the side affected by Parkinson's syndrome the range of the swinging is less than on the healthy side. When both sides are affected the diminution of swinging runs parallel to the rigidity. However, quite the opposite prevails in a cerebellar affection. Here the range of the swinging is greater on the affected than on the healthy side.

(*b*) *Arm-dropping Test.*—The examiner, standing in front of the patient, puts his hands on the sides of the patient's trunk, dorsum outward, at the level of the wrists. The patient is made to relax. With a sudden, quick, outward movement the examiner thrusts the patient's arms up and allows them to fall and strike the dorsum of his own hand. The examiner sees, feels, and hears that the impact of the falling arm on the side affected with Parkinson's syndrome is slowed up and not as heavy as that on the healthy side. The more the side is affected the softer and more retarded is the impact of the falling arm.

(*c*) *Pendulousness of the legs* (as described above).

A tremor may show the greatest similarity to Parkinson's syndrome, but when the head-dropping test and these three tests are normal then the syndrome can certainly be excluded. Thus far I have not seen any case of Parkinson's syndrome of any degree, of any variety, in which the head-dropping test was normal.

Head-dropping Test in Extrapyramidal Diseases

Since the neck muscles are a place of predilection in many other affections of the extrapyramidal system, it is understandable that an abnormal head-dropping test is found in such extrapyramidal conditions as Wilson's disease, torsion dystonia, striatal torticollis, and pallidal degeneration. Thus the dropping of the head as seen in Parkinson's syndrome indicates involvement of the neck muscles in extrapyramidal affections and even the degree of this involvement. It has proved helpful in cases of cortico-striato-spinal degeneration belonging to the group of spastic pseudosclerosis, and of olivo-ponto-cerebellar atrophy, pointing to the existing extrapyramidal component in these diseases. Generally speaking, a pathological head-dropping test in any complicated morbid condition indicates concomitant involvement of the extrapyramidal system.

We have thus far learned *one* outstanding characteristic of the head-dropping test: it shows striking changes in affections of the extrapyramidal system. There is another feature of this test which makes it valuable for differential diagnosis of extrapyramidal and pyramidal affections; it is that the head-dropping test does *not* show any marked or substantial change in pyramidal affections, not even in those in which both pyramidal tracts are affected intracranially.

A completely or nearly completely normal head-dropping test has been observed in patients with bilateral pyramidal lesions, which include an involvement of the pyramidal cortico-cervical tracts. These were cases of spastic tetraplegia with positive snout reflex, positive head retraction reflex, and markedly exaggerated jaw reflex. Some cases showed marked supranuclear bulbar ("pseudobulbar") signs and pathological laughing and crying. The common hemiplegia, of course, also shows a normal head-dropping test, and so does any affection of the cerebellum.

This being so, a pathological head-dropping test in diffuse affections of the brain points to extrapyramidal involvement. In diffuse hypertensive encephalopathy and in multiple sclerosis there may be such an extrapyramidal component. This can be ascertained and appraised by means of the head-dropping test.

The statement just made, that affections of the pyramidal tracts do not influence the head-dropping test, must be modified somewhat by saying that they do not essentially affect the head-dropping test. Though it is true that cases of marked pyramidal involvement have been seen in which this test was normal, occasionally some modification of it has been seen in pyramidal lesions. But here the downward movement of the head never assumes the same character as that seen in Parkinson's syndrome. It is only somewhat uneven, jerky. However, the problem of the head-dropping test in pyramidal lesions requires further investigation. The minor deviation in the test as seen in pyramidal lesions is infinitely less evident than that seen in Parkinson's syndrome, in which it is so obvious as to be unmistakable. Therefore if in a brain lesion with pyramidal signs the head-dropping test is found as in Parkinson's syndrome, this points to concomitant involvement of the extrapyramidal nervous system.

To sum up: In the head-dropping test, the head of the patient lying supine is suddenly and briskly lifted and dropped by the examiner. A slow hesitant movement or a soft fall, a gentle hitting of the surface, is indicative of a lesion of the extrapyramidal system and constitutes a valuable diagnostic sign in Parkinson's syndrome.

REFERENCES

Brock, S., and Wechsler, I. (1927). *Arch. Neurol. Psychiat., Chicago*, 17, 12.
Gowers, W. R. (1893). *A Manual of Diseases of the Nervous System*, 2nd ed., 2, 646. Churchill, London.
Kraus, W. M. (1924). *Ann. Méd.*, 15, 67.
Lewy, F. H. (1923). *Die Lehre vom Tonus und der Bewegung*, p. 9. Springer, Berlin.
Steck, H. (1926). *Schweiz. Arch. Neurol. Psychiat.*, 19, 195.
—— (1927). Ibid., 20, 92.
Vujic, V. (1949). *Acta med. iugoslav.*, 3, 133.
Wartenberg, R. (1945). *The Examination of Reflexes*, p. 30. Year Book Publishers, Chicago.
—— (1951). *Neurology*, 1, 18.
Wilson, S. A. K. (1940). *Neurology*, 2, 791, 794, 799. Arnold, London.

SIDE-EFFECTS OF A PREPARATION OF VITAMIN B_{12}

BY

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During the course of an investigation involving large numbers of intramuscular injections of a proprietary preparation of vitamin B_{12} (Bedford, 1951a) side-effects were noticed which warranted further inquiry. This preparation was a vitamin-B_{12} "concentrate" derived from *Streptomyces griseus* fermentation liquors, and, being both effective and inexpensive, was assuming increasing prominence in the treatment of pernicious anaemia. It was of interest to determine whether the vitamin B_{12} itself or a contaminant was responsible for these side-effects, and to investigate some factors which may have predisposed to their occurrence.

Method

Three preparations were available for trial: (1) "A" was the proprietary vitamin-B_{12} preparation referred to above, containing 20 μg. per ml. It is described as a concentrate, being in fact a solution of vitamin-B_{12} factors derived from streptomyces fermentation liquors by a combination of customary extraction procedures, and is no longer in general issue (J. T. Marsh, 1951, personal communication). (2) "B" was a proprietary preparation of vitamin B_{12} derived from liver and contained 10 μg. of B_{12} per ml. (3) "C" was a solution of vitamin B_{12a} containing 20 μg. per ml., derived, like A, from streptomyces culture liquors, but "purified by crystallization and therefore likely to contain a smaller proportion of any impurity" (J. T. Marsh).

At the time of this investigation the proprietary preparation which has replaced A in general issue was not available for trial. It is, like C, a streptomyces derivative purified by crystallization, but is a solution of vitamin B_{12} (not B_{12a}), and its impurities are stated not to exceed 1 part in a million millions (J. T. Marsh, 1951; H. M. Walker, 1951: personal communications).

One hundred people (27 women and 73 men) between the ages of 21 and 90 were injected intradermally with 0.1 ml. of A, 0.2 ml. of B, and 0.1 ml. of C—that is, equal doses of vitamin B_{12}—on the flexor surface of the forearm, and the results recorded at 15 minutes, 30 minutes, and 24 hours. Positive reactors were arbitrarily assessed as those with persistent wheals 5 mm. and more in diameter.

Results

The results are set out in Table I. There were 14 positive reactions to A, none to B, and two to C (both of these being also positive to A).

TABLE I.—*Positive Intradermal Tests*

		0·1 ml. A	0·2 ml. B	0·1 ml. C
Men	73	9	0	1
Women	27	5	0	1
Total ..	100	14	0	2

Of the 100 people under test, 52 had received one or more antibiotics within the past five years (49 penicillin, 7 streptomycin, 4 "aureomycin," and 2 chloramphenicol), while 48 denied previous contact with mould products. Table II illustrates the relationship between skin-test positive reactions and previous treatment with antibiotics. Of those who had previously received antibiotics, 19% were skin-test-positive to A, whereas only 8% of those who had *not* previously received antibiotics were A-positive.

TABLE II.—*Relation Between Positive Intradermal Reactions and Previous Antibiotics*

	Previous Antibiotics	A-positive	C-positive	No Previous Antibiotics	A-positive	C-positive
Men ..	43	6	1	30	3	0
Women ..	9	4	1	18	1	0
Total ..	52	10 (19%)	2	48	4 (8%)	0

As the relationship between positive intradermal reactions and general sensitivity phenomena is not absolute, it was decided to estimate directly the proportion of people who might be expected to exhibit side-effects to A, B, and C when these were administered, as is usual, by deep intramuscular injection. Two groups of people were selected, group 1 being the 14 skin-test A-positive reactors, and group 2 being 14 skin-test A-negative reactors. They were injected with 2 ml. of A, 4 ml. of B, and 2 ml. of C—that is, 40 μg. of vitamin B_{12} in each case—as follows:

Experiment 1: 2 ml. of A to group 1, and 2 ml. of A to group 2; followed two days later by *Experiment 2:* 4 ml. of B to group 1, and 4 ml. of B to group 2; followed two weeks later by *Experiment 3:* 2 ml. of C to group 1, and 2 ml. of C to group 2; followed after a further two days by *Experiment 4:* 2 ml. of A to group 1, and 2 ml. of A to group 2.

The results are set out in Table III. As experiments 2 and 3 yielded no reactions they are omitted from the table; the results of experiments 1 and 4 were identical and so are not set down separately. There were no side-effects to B or C, but six cases reacted adversely to A. There were two moderately severe reactions (both in group 1), consisting of considerable pain and tenderness at the site of injection, with fever, shivering, and malaise beginning six hours after the injection and lasting 24 hours. Four mild reactions occurred (two in group 1, and two in group 2), consisting of pain and tenderness at the injection site lasting 24 hours.

TABLE III.—*Side-effects to A in Positive and Negative Skin Reactors*

Side-effect of 2 ml. A Intramuscularly	A-positive	A-negative
Moderate	2	0
Mild	2	2
Nil	10	12
Totals ..	14	14

Table IV illustrates the relationship between previous antibiotic treatment and the occurrence of side-reactions, and is based on experiments 1 and 4 above—that is, on 28 people. Of those who had previously received antibiotics 26% developed side-effects to intramuscular injection of A, whereas only 11% of those who had *not* previously received antibiotics reacted adversely.

TABLE IV.—*Relation Between Side-effects to A and Previous Antibiotics*

	Previous Antibiotics		No Previous Antibiotics	
	No.	Side-effects	No.	Side-effects
Men	13	3	6	1
Women	6	2	3	0
Total ..	19	5 (26%)	9	1 (11%)

Conclusions.—Although the numbers involved in these experiments are too few to be statistically evaluated, the following inferences may be drawn: (1) It is clear that the factor responsible for both the sensitivity reactions and the

side-effects was not vitamin B_{12} but an impurity present in A, absent in B, and present in traces in C. This substance was therefore probably a carry-over impurity from the streptomyces fermentation liquor (Tables I and III). (2) People who had previously received penicillin or other antibiotics were more than twice as likely to be skin-sensitive and to develop side-effects to the "mould impurities" as those who had not been so treated (Tables II and IV).

Discussion

There is increasing evidence that unusual responses to antibiotic therapy are nearly always the result of acquired sensitivity (*Lancet*, 1951), and that non-specific hypersensitivity to fungi or mould-products may be responsible for a significant proportion of these unusual responses. The conclusions above imply an antigenic relationship between antibiotics and carry-over impurities in certain vitamin-B_{12} preparations derived from streptomyces: it is a reasonable corollary that the converse relationship is valid.

In themselves, the side-effects and skin reactions described above, being trivial, would be scarcely worthy of mention were it not that they indicate yet another way in which idiosyncrasy to antibiotics may be acquired. Deaths directly due to this cause are very rare, but it may prove a serious handicap in the management of infections, since people who are idiosyncratic to one antibiotic may be sensitive to all the others (Bedford, 1951b) and reactions may be so severe that antibiotic therapy becomes impossible.

This investigation does not exclude the possibility that preparations of vitamin B_{12} derived from liver may also contain impurities capable of producing sensitivity phenomena (nor, indeed, that the pure vitamin itself may be capable of doing so); but there is no evidence that sensitivity to liver derivatives implies idiosyncrasy to antibiotics.

Cogent reasons for preferring any preparation of vitamin B_{12} to liver extracts were low price, greater purity, relative freedom from side-effects, and the trivial nature of these when they did occur. As, however, there are now available highly purified vitamin-B_{12} preparations from both liver and streptomyces, against which no evidence of liability to promote idiosyncrasy to antibiotics has been adduced, the use of the cruder mould-derivatives is unjustified.

Summary

Of 100 people 14 were skin-test-positive to a vitamin-B_{12} concentrate derived from *Streptomyces griseus*, and six suffered side-effects after intramuscular injection.

Two were skin-test-positive to a purer preparation of vitamin B_{12} derived by crystallization from streptomyces cultures, and none developed side-reactions to intramuscular injection.

None reacted adversely to a preparation of vitamin B_{12} derived from liver.

Impurities carried over from the mould fermentation liquor are regarded as responsible for the sensitivity phenomena.

Both cutaneous reactions and side-effects were more than twice as common in people who had previously been treated with antibiotics.

The possibility of inducing idiosyncrasy to antibiotics is advanced against the use of impure preparations of vitamin B_{12} derived from mould cultures.

It is with great pleasure that I express my gratitude to Mr. J. T. Marsh and Dr. H. M. Walker, of the Medical Department of Glaxo Laboratories Ltd., for supplies of vitamin-B_{12} preparations and for information concerning them; and to the patients and staff of the Cowley Road Hospital for their co-operation in this investigation.

REFERENCES

Bedford, P. D. (1951a). *Lancet*, 1, 1232.
—— (1951b). *British Medical Journal*, 1, 1428.
Lancet, 1951, 2, 24.

"EPIDEMIC" ABDOMINAL COLIC ASSOCIATED WITH STEATORRHOEA

BY

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Many specimens of faeces from cases of gastro-enteritis and diarrhoea suspected of being infective in origin are sent to the laboratory for examination. Often a known bacterial or protozoal pathogen is found, or food-poisoning organisms are incriminated; but a number of sporadic cases and a few epidemics remain for which no satisfactory explanation is found. We have observed the occurrence of pale stools and steatorrhoea among some of these unexplained cases, and an outbreak of gastro-enteritis of this kind is described here because it suggests the occurrence of a syndrome of infective intestinal disorder which is not generally recognized.

The Outbreak

In December, 1950, a number of cases of diarrhoea occurred in a day nursery accommodating 50 children under the age of 5. The course of events is summarized in the Table. After the tenth day no further cases of diarrhoea or vomiting occurred. It will be seen that fresh cases developed over a period of nine days. In all, 25 children aged from 1 to 4 years and six staff were affected—just under half the number of persons at risk. In addition four household contacts of three children (Cases 2, 3, and 6) were affected. These secondary cases developed from two to four days after the onset in the child concerned.

Day of Outbreak	Case No.	Sex	Onset of Symptoms
1	1	M	Diarrhoea during night
2	2	F	" and vomiting in morning
2	3	M	" " " "
2	4	F	" at midday " "
3	5	M	Severe stomach-ache in afternoon
3	6 to 16		Diarrhoea beginning at various times during the day. Case 13 had also severe vomiting
4	17	F	Diarrhoea
5	18	M	Diarrhoea.
5	19 to 22		Four of the staff complained of abdominal pain and flatulence with a sensation of "churning up" in the intestines.
6	23	F	Diarrhoea
6	24	M	Diarrhoea.
6	25 to 26		Two more of the staff felt ill
7	27	M	Diarrhoea and vomiting
7	28	F	" " "
7	29	M	Diarrhoea
8	30	M	"
9	31	M	Vomiting
10			Case 6 suffered from vomiting. She had been well for the three previous days Case 8 had diarrhoea again. He had been well for the five previous days Case 3, who had been ill for four days and better for four days, developed a second bout of diarrhoea

Clinical Picture.—The clinical picture was characteristic. The affected children showed a striking pallor with the onset of symptoms, and pain in the abdomen or vomiting (five cases) was the first complaint. The urgency of the call to stool and the apparent straining were severe, out of proportion to the degree of the diarrhoea; and a few children who cried for their pots failed to pass any faeces. The adults who were affected suffered from abdominal pain, flatulence, and nausea, and felt ill; but no adult had frank diarrhoea.

No case was ill for longer than four days, but three cases relapsed and had a second bout of diarrhoea or vomiting a week after the onset of their first attack. Six of the children had slightly raised temperatures. One child had jaundice a fortnight after his diarrhoea.

Laboratory Findings

Stool specimens from 24 of the 25 affected children were sent to the laboratory on the first or second day of illness. It was noticed at once that 17 of these were unusually pale in colour, and most were fluid. Fourteen were given careful microscopical study as well as a bacteriological examination; 10 were examined bacteriologically only. The bacteriological examination included a special search for heat-resistant strains of *Cl. welchii*, and for *Bact. coli* of the possibly pathogenic D 433 and "Aberdeen beta" types; but these organisms were not found; nor were shigellae or salmonellae. All organisms isolated were recorded; but not one organism of any kind was common to even a majority of cases. It thus appeared that no help could be obtained from the bacteriological examination; and attention was redirected to the microscopical findings. No cysts, worms, ova, or protozoa had been found, and no leucocytes or red cells; but globules of neutral fat (staining with Sudan) had been seen in 9 of the 14 cases examined microscopically. These globules were mostly from 10 to 30 μ in diameter, and were numerous in every microscopical field.

Castor oil, paraffin oil, and cod-liver oil were considered; but the first two had not been given; and faeces specimens from children from another nursery, in which a similar diet and the same amount of cod-liver oil were being given, did not show this undigested fat.

It therefore seems that steatorrhoea was an abnormality associated with the outbreak of gastro-enteritis described, and that the characteristic stool was pale or putty-coloured, fluid, and acellular, with, in most cases, much undigested fat recognizable microscopically.

Discussion

A great deal of gastro-enteritis occurs in the community, and often no attempt is made to obtain an explanation. When multiple cases occur within an institution, however, a single cause is reasonably suspected and it is usual for some investigation to be made.

In the majority of such outbreaks referred to this laboratory shigellae, salmonellae, or Giardia have been incriminated; but in four recent incidents of the kind, including that described above, no pathogen was isolated from the faeces and the circumstantial evidence did not suggest food-poisoning. An additional search for heat-resistant *Cl. welchii* and for *Bact. coli* of types associated with infantile enteritis was without result. It was noticed, however, that the stools of these patients were often of a pale putty colour, and that on *microscopical examination* leucocytes were almost always absent, however fluid the faeces, while globules of undigested fat were quite often present in specimens from children.

The occurrence of multiple cases of this condition, some of which exhibited fever over periods of four days, suggested an infective agent, but the negative results of many bacteriological examinations imply that the organism, if it exists, is not easily cultivated, and perhaps a virus aetiology should be considered.

The disorder would seem to have affected the digestion of fat in the small intestine, since it started as central abdominal colic with flatulence and was often followed by the passage of pale fatty stools. The absence of leucocytes indicated that there could not have been much inflammation of the large bowel mucosa.

In addition to the minor epidemic incidents referred to, sporadic cases of gastro-enteritis with similar features have been encountered, but in these isolated cases many explanations are possible, and such conditions as subicteric infective hepatitis, idiopathic steatorrhoea, and unsuitable diet have to be considered in diagnosis. It would be of value in such cases, and especially when they occur in outbreaks, to have a biochemical analysis of the stools, and to examine blood and urine for bile factors. Bile has not been found so far in a few urine specimens from similar cases.

The syndrome can be recognized. Further observations are needed to determine whether it is rare or common, and to throw light on its cause or causes.

DEATH FOLLOWING A BARIUM ENEMA IN A CHILD WITH HIRSCHSPRUNG'S DISEASE

BY

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It is generally recognized that barium enemata must be given with caution in cases of megacolon, because of the danger of precipitating intestinal obstruction. The following is an account of a case in which a child suffering from megacolon died after a barium enema, but from a different cause.

Case Report

The patient, a boy aged 3 years and 10 months when he was admitted to hospital on November 28, 1949, was the third child of healthy parents. The family history revealed nothing of any significance. There was no previous history of fits in the patient or in the family. He had been constipated since birth and had regularly been given soap suppositories. With this stimulation a hard brown stool was passed every three or four days.

Examination showed that the abdomen was grossly distended and tympanitic. In contrast, his limbs were wasted. His weight was 35 lb. (15.9 kg.). No other abnormalities were discovered. Before a barium enema he was given soap enemata daily. Less than 1 pint (570 ml.) of fluid was given on each occasion without ill effect. His bowel appeared to have been satisfactorily cleared of faeces on the day of the investigation, although the abdomen was still distended.

Four pints (2.3 litres) of barium emulsion was introduced and the *x*-ray films showed the typical appearance of Hirschsprung's disease with a short aganglionic segment. An attempt was made to siphon back the emulsion without result, and on return to the ward it was noticed that the child's condition was unsatisfactory. He was cold, collapsed, and sweating. In an effort to retrieve the enema emulsion, a soap enema of 1½ pints (850 ml.) was introduced, but this too was retained. The sweating persisted and he began to vomit dark-coloured fluid. About seven hours later he lapsed into coma, became cyanosed, and began to have generalized convulsions. This condition persisted through the night and sedatives were given repeatedly. It was noticed that large quantities of very dilute urine (S.G. 1001) were being passed. Examination of the central nervous system at this stage showed no abnormal physical signs apart from the unconsciousness, dilated pupils which reacted sluggishly to light, and bilateral Babinski reflexes. He eventually died in a convulsion 20 hours after the enema had been given.

Permission for necropsy was not obtained, so the cause of this sudden death cannot be proved with certainty, but it seems probable that it was due to water intoxication.

Discussion

In this connexion Rowntree (1926) demonstrated certain phenomena in man and in experimental animals. If a patient with diabetes insipidus began treatment with pituitrin but did not at the same time limit his excessive water intake

he developed weakness and vomiting. If large amounts of water were given to normal dogs by stomach tube they developed retching, vomiting, and violent convulsions, ending in death. The only abnormality found after death was oedema around the cerebral blood vessels. Rowntree also found that the convulsions could be prevented by cerebral decompression operations.

Helwig, Schutz, and Curry (1935) reported the case of a woman aged 50 who by mistake received 9,000 ml. of water by proctoclysis in 30 hours. She became ill with sweating, vomiting, and pain in the neck. She passed into a stupor about 20 hours from the beginning of the symptoms and died 13 hours later after a series of convulsions. At necropsy the lungs and cardiovascular system were normal; the dura was very tense and the brain oedematous, with convolutional flattening. Microscopy showed perivascular oedema.

More recently, Hiatt (1951) noticed that patients with megacolon suffered from sweating, anorexia, and weakness following enemata. He showed that the rate of absorption of water from the colon was dependent on the intraluminar pressure, hence the symptoms were precipitated by straining, and investigations of the plasma electrolytes revealed that these symptoms were accompanied by a sudden marked drop in the sodium and chloride concentrations.

In the absence of any other satisfactory reason for death, it appears probable that this child died from water intoxication. The weight of Helwig and Schutz's patient is not stated, but if, for the sake of argument, it is assumed to have been 140 lb. (63.5 kg.) the lethal amount of water in her case was 9,000 ml. given in 30 hours. The equivalent amount for a child of 35 lb. (15.9 kg.) would be 2,250 ml. The child here reported received 3,124 ml. in a few hours. The symptoms and signs were those of water intoxication. The possibility of barium poisoning was investigated; no soluble barium salt could be found in the mixture that was used, and the solubility of barium sulphate is so slight that a toxic dose could not be dissolved in 4 pints (2.3 litres) of water.

The danger of water intoxication must be remembered when enemata are given to children with megacolon. The volume of the enema fluid must be limited, and every effort be made to retrieve it. Hiatt suggests using isotonic salt solution, which, if absorbed, will not tend to cause cerebral oedema; but an increase in the circulating blood volume will result, which could conceivably produce pulmonary oedema. He suggests that the fluid could be made hypertonic by adding some innocuous non-diffusible substance, say 7% gelatin.

The symptoms of water intoxication are due to the increase in interstitial and intracellular fluid. Treatment of an established case should aim at causing a shift of this fluid back into the circulatory system. The treatment recommended is the transfusion of hypertonic saline, and the amount of sodium ion that is needed can be calculated if the volume of absorbed water is known.

If circulatory failure occurred owing to a rapid increase in circulating volume a venesection would be necessary.

I wish to express my grateful thanks to Professor W. F. Gaisford for his helpful criticisms.

REFERENCES

Helwig, F. C., Schutz, C. B., and Curry, D. E. (1935). *J. Amer. med. Ass.*, **104**, 1569.
Hiatt, R. B. (1951). *Ann. Surg.*, **133**, 313.
Rowntree, L. G. (1926). *J. Pharmacol.*, **29**, 135.

W.H.O. and the Rockefeller Foundation have sponsored a pilot survey, to be carried out in England and France, on the types of health and welfare workers best qualified to meet the needs of the family (International Hospital Federation *News Bulletin*, March, 1952). The survey has begun in Bedfordshire, and will be extended to London shortly; work is also progressing in France.

Medical Memoranda

Spontaneous Rupture of a Leukaemic Spleen

Although Kaufmann (1929) mentions that a leukaemic spleen may rupture spontaneously such cases are rare enough to warrant being placed on record.

CASE REPORT

A Sinhalese man aged 56 was admitted with the history of pain in the upper part of the abdomen of two months' duration. The pain was continuous and unrelated to meals, but he vomited occasionally after taking food.

On examination he was pale but fairly well nourished. His pulse was 76 and temperature 98.4° F. (36.9° C.). No abnormality was found in the cardiovascular and respiratory systems. There was a hard smooth mass in the left hypochondrium, reaching to the umbilicus, which appeared to be an enlarged spleen. No lymphatic nodes were palpable. *X*-ray examination after a bismuth meal did not reveal any abnormality in the gastro-intestinal tract. The stomach appeared to be in the normal position, but the left kidney was pushed downwards. The leucocytes totalled 26,200 per c.mm., and the differential count showed 16% polymorphs and 84% lymphocytes. Most of the lymphocytes were mature and belonged to the small variety. No malaria parasites were seen in the peripheral blood.

Diaphragmatic surface of spleen.

As the pain became more severe and was unrelieved by any medication, it was decided to explore the abdominal cavity. This was done two days after admission, by a left paramedian incision. There was a fair quantity of blood in the peritoneal cavity. The spleen was found to be considerably enlarged, and several ruptures exposing the splenic pulp were noticed. The lymphatic nodes at the hilum and alongside the splenic artery were also enlarged. The liver was slightly enlarged, but palpation failed to reveal any nodules. He was given 10 oz. (280 ml.) of blood, and splenectomy was carried out by Mr. R. Anthonis.

A blood count one month after the operation showed: erythrocytes, 3,595,000; Hb, 60%; leucocytes, 30,000 (polymorphs 25%, lymphocytes 69%, eosinophils 6%).

Description of Specimen.—The spleen measured 22 by 18 cm. and weighed 1,800 g. There was an extensive rupture exposing a large area of splenic pulp on the visceral surface and adjacent part of the diaphragmatic surface. Two irregular linear ruptures extended from this area towards its upper border, and a triangular-shaped rupture was seen towards its lower pole. The rupture over the diaphragmatic surface involved almost the whole breadth of the viscus (see illustration). Two linear ruptures extended from the splenic notch towards the diaphragmatic surface. The sectioned surface of the spleen appeared nodular. Localized areas of perisplenitis were found on the diaphragmatic surface. Microscopically the pulp was seen to be overrun with closely packed lymphocytes, which were uniformly distributed, obliterating the Malpighian corpuscles. Numerous mitoses were seen. The lymph sinuses were packed with lymphocytes.

COMMENT

The absence of a history of trauma suggests that this was a case of a rupture occurring spontaneously in a pathologically enlarged spleen. Although the presence of blood in the peritoneal cavity suggests that at least one of the ruptures had occurred prior to operation it is not possible to be certain about the "spontaneous" origin of all the ruptures, as even comparatively mild trauma, which is necessarily inflicted on the viscus during operative manipulation, may be sufficient to cause the rupture of a spleen which is grossly enlarged.

The enlargement of the spleen in this case exceeded that usually seen in cases of lymphatic leukaemia, but the cells in the peripheral blood were undoubtedly lymphocytes, and as they were of the small variety no difficulty was experienced in differentiating them from the cells of the myeloid series.

The absence of infarcts also points to lymphatic leukaemia as being the causative factor in the splenomegaly. The incidence of splenic infarction is much less frequent in lymphatic leukaemia. Lubarsch (1927) records infarcts in only 12.5% of lymphatic cases as against 50% of myeloid cases. There was no evidence of malaria or of kala-azar. It was concluded that lymphatic leukaemia was solely responsible for the splenic enlargement.

My thanks are due to Mr. R. Anthonis, surgeon, General Hospital, Colombo, for the case notes, and to Mr. K. M. M. Michael, of the Department of Pathology, University of Ceylon, for the photograph.

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REFERENCES

Kaufmann, E. (1929). *Pathology for Students and Practitioners*, p. 232. Philadelphia.
Lubarsch, O. (1927). Cited by H. Downey in *Handbook of Hematology*, 1938, 4, 2898. New York.

Torsion of Fallopian Tube during Pregnancy

Torsion of the Fallopian tube is in itself a rare condition; only about 120 cases having been recorded in the past 50 years. Records of this condition occurring during pregnancy are even less common. For this reason, and because of its general interest, the following case is reported.

CASE REPORT

A primipara aged 27 was admitted to hospital on April 26, 1951, complaining of abdominal pain. This pain, which was constant and dull in character, was situated in the right iliac fossa and radiated across the abdomen and round to the back. It had been present for approximately 60 hours, originally awakening her in the night. During the previous six hours it had become more severe. Vomiting occurred on two occasions on the first day of her illness. Her bowels had been constipated and she had nocturia and painful micturition for two days. No previous history was obtained of a similar pain or of any previous illness. Her last menstrual period started on September 12, and she therefore appeared to be 32 weeks pregnant. Her pregnancy up till then had been uneventful. She had been attending an antenatal clinic regularly.

On examination her tongue was furred. She was tender above the right inguinal ligament, although not markedly so. There was no tenderness in either loin. The size of the uterus appeared to be much in advance of her dates. Rectal examination, although causing discomfort, was negative. On vaginal examination a soft mass was felt in the right iliac fossa outside the uterus.

On admission the temperature was 99.4° F. (37.4° C.) and the pulse 80. In four hours her temperature had risen to 100.4° F. (38° C.) and her pulse to 100. A catheter specimen of urine revealed an acid reaction with a trace of protein. The deposit contained a few pus cells and a very occasional red cell. A provisional diagnosis of acute appendicitis was made and operation was decided upon.

The abdomen was opened through a right pararectal incision. A large mass was palpated in the right iliac fossa, and the right Fallopian tube was gangrenous in its whole extent. Its removal was impeded by the size of the uterus, and its congestion caused bleeding difficult to control. A gauze pack was inserted into the right iliac fossa.

The surgical post-operative course was uneventful and the gauze was removed on the second day. Morphine was given to prevent the onset of labour, but on the fourth night after operation labour began. The patient was transferred to a maternity unit four days after operation. At this time labour was well advanced and the membranes had ruptured. The cervix was dilated to two fingerbreadths and the head was in mid-cavity. A Danby belt was applied to give support to the abdominal wound. Labour progressed slowly, and four hours later the cervix became fully dilated. An episiotomy was performed because of delay in the second stage due to a rigid perineum, and a live male infant weighing 8 lb. 2 oz. (4.2 kg.) was delivered.

The puerperium was uneventful, and both the abdominal wound and the episiotomy healed well. When seen one month later both patient and baby were well.

Pathology.—The right Fallopian tube measured about 3 by 2 in. (7.5 by 5 cm.) and was very congested. A single twist had occurred at the proximal end of the isthmus. Sections showed complete infarction.

COMMENT

Only two cases of torsion of a normal tube in pregnancy have previously been reported in the English literature (McKerrow, 1934; Caldwell, 1949). Twisting of a hydrosalpinx or a haematosalpinx during pregnancy occurs more often. Green-Armytage (1929) and Sheldon (1936) reported cases of torsion of both the Fallopian tube and the ovary during pregnancy; but in our case the ovary was not involved. All cases reported were operated upon as acute appendicitis, and thus laparotomy is necessary for diagnosis. Pyelitis and twisted ovarian cyst are other conditions that have to be considered in the diagnosis.

It was noticed that the site of pain was low in the right iliac fossa. The pain of appendicitis in pregnancy is usually higher up in the abdomen owing to the displacement of the appendix by the enlarging uterus. Because of this an incision was made over the site of maximal tenderness.

It is obvious that the patient was mistaken in her dates. One must assume from the weight of her child that the pregnancy was considerably more advanced than had been thought. In the two cases previously referred to the condition occurred at about the sixth month and pregnancy then went on to term. Our patient was stimulated into labour. The good ultimate result in both patient and child is noteworthy.

We wish to thank Mr. S. B. Chambers, senior surgeon, Royal South Hants Hospital, for his permission to publish this case; Mr. R. W. Knowlton, obstetrician; and Dr. H. H. Gleave, pathologist, for his report on the specimen.

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REFERENCES

Caldwell, R. K. (1949). *New Engl. J. Med.*, 240, 421.
Green-Armytage, V. B. (1929). *J. Obstet. Gynaec. Brit. Emp.*, 36, 87.
McKerrow, W. (1934). *British Medical Journal*, 1, 850.
Sheldon, D. (1936). *Amer. J. Obstet. Gynec.*, 31, 682.

Reviews

UROLOGY OF CHILDHOOD

The Urology of Childhood. By T. Twistington Higgins, O.B.E., M.B., Ch.B., F.R.C.S., D. Innes Williams, M.D., M.Chir., F.R.C.S., and D. F. Ellison Nash, F.R.C.S. (Pp. 286; 136 figures. £2 5s.) London: Butterworth and Co. 1951.

The authors have indeed made an outstanding contribution to urology by presenting, in the light of the most recent advances in this specialty, the wealth of clinical and pathological material which has been collected at "Great Ormond Street." A summary of the physiology of micturition serves as an admirable introduction to the aetiology and management of incontinence and enuresis as shown by investigations into habit, by cystometry, and by electroencephalography. The account of the management of infections of the urinary tract includes much valuable information on the newest sulphonamides and antibiotics and on their side-effects. The authors then consider the association of medical and surgical diseases of the kidney jointly as they affect the renal parenchyma and hence the biochemistry of the body. The chapter on embryology not only gives information on many of the most controversial points in the development of the urinary system, but helps to explain very clearly congenital abnormalities of the upper and lower urinary tract. The effects of urinary obstruction are discussed at three levels: vesical retention due to obstruction at the bladder neck, posterior urethral valves, and abnormalities of the urethra; obstruction at the uretero-vesical level in the various types of mega-ureter; and obstruction of the upper urinary tract causing hydronephrosis. Each chapter is illustrated by photographs of specimens and by radiographs from the unique collection in the museum of that hospital. Likewise, in the chapters on urolithiasis, urinary tuberculosis, and neoplastic disease the authors make admirable use of the immense amount of pathological and radiological material at their disposal. The book is also a practical one in that the authors give detailed descriptions of the technique of investigation, management, and operative procedure.

This work will be of the greatest assistance to all who require an authoritative textbook on the urology of childhood and also to those wanting to obtain references to the more recent advances in this specialty.

J. E. SEMPLE.

CLEFT LIP

Cleft Lip and Palate. By W. G. Holdsworth, F.R.C.S.Ed., F.R.C.S. With foreword by Sir Harold Gillies, C.B.E., F.R.C.S. (Pp. 126; 87 figures. £1 15s.) London: William Heinemann Medical Books. 1951.

Textbooks of surgery tend to fall into two distinct classes—those whose aim is to help candidates through examinations, and those concerned with the actual treatment of cases. In the former it is necessary to set out all known varieties of treatment and hypotheses of pathology without recommending one or attacking others; for who can say whether the examiner will approve of a definite opinion on one side of a debated question? Because so many points of view have to be stated, such a book has to treat each one very shortly or become of an impossible length. The second type of textbook tends to be argumentative, opinionated, and detailed, confining its remarks on all theory and practice outside that of the author to pointing out how wrong they are. The dust cover of Mr. Holdsworth's book suggests the category to which it belongs by stating that "questions on these topics constantly arise in Fellowship examinations," and that the operations described in various parts of the world are described and classified. In consequence his book invites criticism from the point of view of the examinee rather than that of the operating surgeon.

In the absence of any guidance from textbooks of anatomy or physiology on the actual mechanism of closure of the palate, a dispute exists between those who maintain that the muscles admittedly existing in this region can close and open the nasopharynx and those who have discovered a hitherto overlooked sphincter of abnormal contractility which performs this function. Mr. Holdsworth evidently holds the first view, and states it alone; but anyone omitting to mention the second is running a grave risk in an examination. A similar fundamental point is how exactly the constituents of the lip join to give it the very definite shape and markings seen in the newborn infant. On this again there is no guidance from the embryologists, nor from this book; but the views of Veau and others should be stated, for it is surely logical first to identify the process that has failed before trying to complete it.

Various formulae for closing single and double clefts of the lip are set out, but the series of drawings would be rather exasperating to an actual operator. This is because the clefts are all shown before operation with a symmetrical pair of nostrils, and the results of various classical flaps and zigzags as the same unvarying normal shape of lip with a perfect cupid's bow. It is an undoubted fault of our present system of surgical education that there is no way of ensuring that (in Army parlance) "this practice will now cease"; though anyone who has to do much of this work knows that some of the formulae here reproduced without comment will set him almost insoluble problems if applied by a trusting general surgeon. The difficult and chancy Abbé operation, for instance, a fine example of which is illustrated here, is one that corrects a man-made deformity, not a congenital one. On the question of the displaced premaxilla in double clefts, there is no definite statement upon whether or not the vomer is of normal length, with a suture-line dividing it from pre-vomerine bone, though this is a question of fact and not of opinion. It is also hard to make out whether or not the premaxilla is to be finally preserved, and if so in what position.

One ends the study of this interesting book hoping that Mr. Holdsworth will abandon in subsequent editions the attempt to help candidates through examinations, in which in any event they will probably be questioned by surgeons whose experience lies in the abdomen, and that he will concentrate upon the clear statement of his own personal opinions and experience. A point on which he might well make a break with the traditions of publications on plastic surgery is to forswear lipstick, retouching, and smiles in illustrations of final results.

DENIS BROWNE.

THE XANTHOMATOSES

Les Xanthomatoses. By A. L. Froehlich. (Pp. 312; illustrated. No price.) Brussels: Les Editions "Acta Medica Belgica." 1951.

This is an important monograph on the xanthomatoses. Like Thannhauser, Dr. A. L. Froehlich, of Antwerp, divides xanthomatoses into those with and those without hyperlipaemia. The first part of the book is on the former, the second part on the latter. Then come the general conclusions (pp. 261–71), a detailed account of 25 original cases (pp. 272–311), and an iconography with 46 histological figures.

Part I is divided into chapters on (1) essential xanthomatosis; (2) essential hyperlipaemia; (3) xanthomata in the course of hypothyroidism; (4) diabetic xanthomata (with a short account of so-called "necrobiosis lipoidica"); and (5) the complicated subject of hepatic xanthomata. Part II, on the xanthomatoses without hyperlipaemia, is divided into chapters on (1) naevo-xantho-endothelioma (McDonagh); (2) intestinal lipodystrophia (Whipple); (3) disseminated xanthomata, including an account of lipoidic proteinosis (Urbach–Wiethe); (4) the Hand–Schüller–Christian disease, and its differential diagnosis including the whole subjects of lipoid-granuloma, xanthomatous changes in fatty tissue, and the xanthomatosis of granulomata and neoplastic tumours.

The author discusses all these subjects and points out that in regard to some questions further observation and the collection of clinical or experimental data are required. Naturally the work of van Bogaert, Scherer, and Epstein on a "Cerebral Form of Generalized Cholesterinosis" (1937) is specially considered. Among the extensive references to much of the older as well as the newer literature the reviewer was much interested to find a case of his own mentioned on p. 207. It was that of a man, aged 37, with diabetes insipidus, who died of pulmonary and laryngeal tuberculosis. At the post-mortem examination a xanthomatous lesion of the posterior part of the pituitary body was found, but there was no other evidence of the Hand-Schüller-Christian disease. Doubtless Dr. Froehlich is right in regarding the case as a very incomplete example of the Hand-Schüller-Christian syndrome. The original description by Parkes Weber and H. Schmidt was published in *Amer. J. med. Sci.*, 1916, **152**, 892.

Dr. Froehlich's book should be kept for reference by all those specially interested in the xanthomatoses and the various theories connected with the subject.

F. PARKES WEBER.

APPLIED ANATOMY

Angewandte und Topographische Anatomie. By Professor Gian Töndury. (Pp. 416; 369 figures. M. 70.) Stuttgart: Georg Thieme. 1951.

In this volume the author aims at combining topographical anatomy, which describes the structure and relationships of the different organs and organic systems of the human body, with applied anatomy, which describes the practical application of this knowledge. Moreover he aims at providing both a textbook for the student and a work of reference for physician and surgeon. That he succeeds in covering this vast field in a moderate compass and in a most brilliant manner is a tribute to the genius of himself and his assistants.

The author is brief, clear, and to the point, and succeeds in including details whose value has only recently appeared in the actual practice of medicine and surgery. I might mention the attention directed to the autonomic nervous system and to the precise anatomy of the intervertebral disks. Short but adequate accounts of morphology and development will be valued by the student as enabling him to understand relationships which would otherwise be incomprehensible.

But the real charm of the book is in the drawings, which are a sheer delight to study. They fall into two groups—line drawings in the text and plates on separate pages. The former are remarkable for their simplicity, appositeness, and perfect draughtsmanship, and indicate close co-operation between the author and his artist, Fräulein Emden. But the plates are supreme examples of achievement in a very specialized field. The artist, Paul Winkler, was himself a medical student, and his drawings show an understanding unattainable by a layman however great his artistic skill. They are from dissections specially prepared and admirably conceived, and are drawn with a supreme technical skill which focuses attention on essential detail while giving an adequate and harmonious background. They are all good, but two drawings of the roots of the lung, one of the posterior mediastinum, one of the abdominal oesophagus, and an enlarged drawing of the inner ear stand out as really superb examples both of representation and of production.

I would suggest that in a future edition a chapter should be added on the anatomy of the child, for the differences are important, and although many are well recognized, as in the cranium and the hip, others are not so well known. For example, the peripheral nerves in a child are almost as large as those in an adult, which is occasionally of great surgical importance. But these are small matters, and the author and his assistants must be congratulated on an achievement which is worthy of the great medical school of Zurich. It will be valued by all who have an interest in the anatomy of the human body.

HENRY SOUTTAR.

INFLAMED INDIVIDUALISM

Between Life and Death. By Harley Williams. (Pp. 288. 16s.) London: Jonathan Cape. 1951.

From John Aubrey through Samuel Johnson to Lytton Strachey the English biographical essay has a long and distinguished history. For the successful practice of this art it is essential that there should be some link between the chosen subjects and some definite plan in each essay. It is here that Dr. Harley Williams's book, good as it is, falls short of success. In a book devoted mainly to the great pioneers of medical research it is as disconcerting to discover Mrs. Eddy in the gallery ("Que faites-vous là, Mary Baker?") as it would be to see Joanna Southcott seated on the bench of bishops; and in an essay concerned with Joseph Lister to find five pages devoted to Lawson Tait is as surprising as it would be to be offered a cigar by the local bookmaker in a meeting of the Society of Friends. Congregations should be congruous, and the flock, particularly when hand-picked, should be of one feather.

If the reader does for himself what the author has failed to do and reads successively the essays on Hunter, Pasteur, Lister, Freud, Ehrlich, and Banting, he will reflect how diverse were the personalities and how various the paths of these remarkable men. They share but one quality—an exclusive intensity of concentration—for, as Emerson wrote, "the excellence of each is an inflamed individualism which separates him the more." These essays are squarely based on the important source books, and it is their merit that they impel one to learn more of their subjects. I am grateful that the chapter on Frederick Banting introduced me to Lloyd Stevenson's biography, the unique story of a man with a mind unprepared for his moment of genius.

Harley Williams is a master of narrative, but occasionally his meaning is obscured in a flurry of words, as when he writes that his sketches are to be judged "as flashes of an old and very remarkable design which is likely to flower again in endless fecund forms." In fact, there are as extraordinary fish in the sea as ever came out of it.

D. V. HUBBLE.

ORTHOPAEDIC NURSING

Orthopaedic Nursing. By Mary Powell, S.R.N., M.C.S.P. (Pp 400; 210 figures. £1 5s., plus 10d. postage.) Edinburgh: E. and S. Livingstone. 1951.

This book, which is dedicated to the memory of the late Dame Agnes Hunt, calls for nothing but praise, for within its covers will be found all that the nurse need know about orthopaedic nursing technique. The text is clear and concise, and the book is generously illustrated with excellent photographs. The emphasis throughout is on splintage and nursing care, and the description of surgical treatment and operations is rightly reduced to a minimum.

It is difficult to single out individual chapters for special mention, but those on plaster-of-Paris technique and on the care of the various types of bone and joint tuberculosis are particularly good. The insistence of Dame Agnes Hunt that there should be no polished floors in orthopaedic wards is noted with approval. It is a pity that all orthopaedic matrons and sisters do not follow this rule. The chapter on the preparation of the patient for examination of the various joints should be studied by nurses doing their general training. The book concludes with an excellent chapter on aftercare by Miss Mona Williams.

J. S. BATCHELOR.

For nearly half a century *Black's Medical Dictionary* (by the late John D. Comrie and Dr. William A. R. Thomson; A. and C. Black, 30s.) has endeavoured to "give information in simple language upon medical subjects of importance and general interest." Twenty editions since 1906 are proof of its reliability as a medical work for the lay public. It is more than a dictionary, for it includes much anatomical description and physiological explanation, fortified by over 400 text illustrations and 16 plates. The whole of the text-matter has been reset.

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FORTY MILLION POUNDS

On Tuesday afternoon, as the *Journal* was going to press, the Minister of Health, Mr. Harry Crookshank, announced in the House of Commons the award of Mr. Justice Danckwerts, the Adjudicator. He stated that the award would mean increases for the years previous to and subsequent to 1950–1. "While, as I say," he observed, "the full calculations have yet to be made, I feel I should inform the House that in very approximate terms this may involve an additional charge on the Exchequer of as much as £40m. in the coming financial year to cover the period back to July 5, 1948. . . . It will be necessary to seek a supplementary Vote for this additional amount."

Thus, nearly four years of discussion, controversy, and protracted negotiations on the remuneration of general practitioners have come to an end with the award of Mr. Justice Danckwerts, the adjudicator appointed by the Lord Chancellor. The medical profession decided to take part in the National Health Service on the clear understanding from Mr. Bevan that their claim for payment could be negotiated immediately after July, 1948. The outstanding point left unsettled was the "betterment" factor. The Spens Report recommended that what general practitioners should have received in 1939 should be scaled up in terms of the altered value of money and in relation to the changed earnings of other professions. In deciding the size of the central pool the Ministry of Health arbitrarily fixed on a betterment factor of 20% on net incomes (that is, after deduction of practice expenses)—something which the profession never agreed to and never accepted. As our correspondence columns have shown throughout these four years, the injustice of this situation has rankled in the minds of general practitioners, and with good cause. With much less cause, but perhaps understandably, some have laid the blame for the delay on those responsible for presenting the profession's case.

Details of the award and a report of the proceedings are given in this week's *Supplement*. Mr. Justice Danckwerts's award brings to an end one chapter in the history of the N.H.S. He has applied for the year ending March 31, 1951, a betterment factor of 100% to the 1939 figure for what general practitioners, in the view of the Spens Committee, should have been receiving then. The amount actually paid for that year was £41.533m.: Mr. Justice Danckwerts's awarded figure is £51.252m. This means that the central pool from which general practitioners were paid on a capitation basis is for 1950–1 to be increased by just under £10m. For 1948, the first year of the operation of the N.H.S., Mr. Justice Danckwerts has recommended a betterment factor of 85%. The factor for 1949–50 will presumably lie somewhere between 85 and 100%, to be determined on the basis of Mr. Justice Danckwerts's awards. Similarly, the same process will be applied to the figure for 1951–2–3. The important point is that general practitioners will receive additional payment back to 1948.

The medical profession's case has been presented so consistently and so cogently that they have gained other and considerable points of principle. First and foremost, Mr. Justice Danckwerts has based his award not on the population but on the number of doctors in the National Health Service. Though this is a logical application of the Spens Report, which sought not to determine a figure for the central pool but to recommend what ranges of income doctors should receive, it was opposed by the Ministry of Health. Another point of variance between the B.M.A. and the Ministry was the inclusion of interest on compensation in their estimate of doctors' total incomes. This again would seem to be, on common-sense grounds, untenable, and Mr. Justice Danckwerts has excluded this figure from consideration, and also the amount of the inducement fund, in his determination of the size of the central pool. As those who have followed the tortuous discussions between the B.M.A. and the Ministry know, there has been disagreement on the percentage for practice expenses. Mr. Justice Danckwerts has accepted the B.M.A. figure of 38.7%, although he adds that he has not "accepted entirely the figures to which this percentage should be applied."

Both the B.M.A. and the Ministry of Health agreed in advance to accept the award of the adjudicator, but it is Parliament which has, and must have, the control of the public purse. The amount of money to be distributed on the basis of the award is considerable, especially as payment will have to be made retrospective to 1948. There can be no doubt that during the past four years the just claims of general practitioners have received growing support both in the Press and in Parliament. It may even be argued that the long delays in negotiation, which have been no fault of the B.M.A., have turned out to be beneficial. This delay has at least allowed public opinion—always slow moving—to turn in sympathy towards the hard-working general practitioner—a sympathy which has found its echo in the House of Commons. What is fundamental to the whole case is the final acceptance of the recommendations of the Spens Report. The Spens Report laid down a standard of living for an important section of

the community, and though the Ministry of Health accepted this in the word its arbitrary decision on a betterment factor of 20% on net incomes, applied to a pool of money based on population and not on numbers of doctors, showed that it did not accept it in spirit. It must be stressed again that both sides entered adjudication on the understanding that they would accept the decision "subject to the overriding authority of Parliament." In the future the extra money awarded will be distributed according to a scheme to be agreed by the Working Party, the G.M.S. Committee's representatives on which will act on the authority of the Conference of Local Medical Committees.

No doubt there will be a few voices protesting that the B.M.A. should have got the betterment factor of 120% claimed for 1951. If such there be, they will have ignored the essential feature of arbitration, which is arbitrament on evidence given by two sides to reach a fair and just decision. But we are confident that the great bulk of the profession will acclaim the efforts of those who have conducted these negotiations on their behalf. These efforts have been brought to a successful conclusion by first-class teamwork and by the able presentation of the profession's case by Mr. Frederick Grant, Q.C., and his colleagues. The burden of the work has fallen, in particular, upon Dr. S. Wand, Chairman of the G.M.S. Committee and Chairman of the Representative Body, and upon Dr. D. P. Stevenson, Secretary of the G.M.S. Committee and Deputy Secretary of the B.M.A. Those who have joined with them in this arduous task will not hesitate to acclaim their services.

The additional money to be paid in retrospect back to 1948 can be distributed only in accordance with the then method of distribution. Future payments will be on the basis now being discussed with the Ministry of Health by the joint Working Party set up to examine the distribution of general practitioners' remuneration. The Working Party's aim is to secure the best possible medical service for the public, to safeguard the standard of practice by discouraging unduly large lists, to improve the position of those practitioners now least favourably placed, to make it easier for new doctors to enter practice, and to stimulate group practice.

Now that the controversy on finance between the B.M.A. and the Ministry of Health has come to an end with the award of the adjudicator they will be able to tackle these and other problems in a spirit, we may hope, of co-operation and mutual respect. Both, after all, have a common aim, and that is to provide the best possible general medical service for the public and to ensure that in the achievement of this those providing the service will be able to do so with freedom from financial anxiety and the feeling of contentment that arises from a just treatment of their claims. The problems to be solved are many and urgent, and towards the solution of these the General Practice Review Committee of the B.M.A. will make an important contribution. In what should be a new spirit of confidence and satisfaction the medical profession will the more easily turn its energies into fulfilling the intention of the B.M.A. as expressed by the then Chairman of Council, Dr. H. Guy Dain, in a letter to *The Times* in June, 1948, in which he said, after pointing out difficulties and deficiencies: "But in spite of all this, I believe I speak for the overwhelming majority of the medical profession when I say that there will be no shortage of good will on the part of the profession and that it will seek to make the new public service the best which is humanly possible under present circumstances. . . . Only the best is good enough for the public service, and we shall do our utmost to provide it."

RETROLENTAL FIBROPLASIA

If anyone doubts that diseases hitherto unexplained are more likely to arise from a set of interlocking factors than from a single cause let him study the literature on retrolental fibroplasia. There he will find interpretations which, though simple and at first acceptable, soon broke down under the impact of new facts. Retrolental fibroplasia was originally assumed to be a congenital defect, but this point of view was contradicted by emergence of the blindness in infants who, having betrayed no ophthalmoscopic abnormality on examination soon after birth, later developed the characteristic fundus changes. When reports of retrolental fibroplasia began to multiply, many people thought that modern advances in the care of prematurely born babies accounted for the increase. In other words, the potential victims of former times had not survived long enough to develop the disease. Such an explanation was manifestly insufficient, because very few cases appeared in Switzerland, a country in which the premature infant is tended with great vigilance. During the discussion on Reese's[1] paper at the last International Congress of Ophthalmology Franceschetti and Blum (Geneva) both testified to the rarity of retrolental fibroplasia in their country.

Hopes were raised a few years ago by the work of Owens and Owens,[2] who claimed that prophylactic administration of vitamin E had prevented retrolental fibroplasia in prematurely born babies of low birth-

[1] *Proc. XVI Int. Cong. Ophthal.*, 1950, 445.
[2] *Amer. J. Ophthal.*, 1949, **32**, 1.
[3] Ibid., 1951, **34**, 1.

weight, whereas numerous victims were found among a series of similar subjects not receiving this substance. Several observers failed to obtain this result when they made controlled investigations in the hope of conferring protection with vitamin E, and it must be admitted that no immediately decisive cause or cure of retrolental fibroplasia has yet been identified. Prematurity and reduced birth-weight are of obvious aetiological significance, but evidently they are not the only factors, otherwise the incidence of the disease would roughly correspond in the large groups of cases which have come under scrutiny. The figures, however, show wide discrepancy, not only between different countries but also between separate regions of the same country. Nor do the results of therapy seem consistent. Some authorities have claimed remarkable success from the use of A.C.T.H., and others have found this drug ineffective. Unless the problem of aetiology is solved, it seems doubtful whether retrolental fibroplasia can ever be prevented or arrested, because the chances of discovering effective empirical remedies must surely be remote.

Meanwhile vivid clinical descriptions have been published, and premature infants have been exhaustively scrutinized to ascertain the earliest ophthalmoscopic signs. All the resources of morbid histology have been mobilized, especially by Reese and Blodi,[3] whose beautiful illustrations and clear account of the disease deserve close study. Among paediatricians and ophthalmologists retrolental fibroplasia has to some extent usurped the attention lately directed upon toxoplasmosis and rubella. General practitioners are closely concerned with the problem, although they seldom have the opportunity to see retrolental fibroplasia in its earliest stages because the sufferers are usually assembled in special units for premature infants. It is hoped that the questionary recently launched by the Medical Research Council will gather helpful information, and certainly the records of maternity departments, premature infant centres, and ophthalmic units are being sifted with care. Dr. B. A. Bembridge and the other members of a research team in Oxford have supplied a helpful review of retrolental fibroplasia elsewhere in this issue, as well as adding further observations of their own. They rightly draw attention to the differences between infantile and adult ocular fundi, and to the fallacies that may be perpetrated by those who ignore these differences. Although they have to admit that the cause of the disease remains a mystery, their work will perhaps not be in vain. Unless the problem is solved by a flash of that intuitional brilliance with which clinicians have often illuminated medicine in former times, many other paths of investigation will have to be followed before this new scourge can be understood and suppressed.

MENTAL HEALTH RESEARCH FUND

In research into mental disorder the fields of study stretch out invitingly on every side; and in the present state of knowledge it is exceedingly difficult to forecast which would be the most profitable to explore. Speculation on these matters is rather like divination, as Professor Aubrey Lewis said at a conference in Oxford last week, but he added the warning that direct attack on problems which seem to be most urgent are not necessarily warranted if contingent knowledge and methods are not ripe. It follows that in this branch of medical research the sharing of knowledge, leading to its integration, is of exceptional importance. The pressing need for integration can be judged from the fact that "in the relatively restricted sphere of electro-encephalography alone there are now a little over three papers a day being published, and in all the subjects which are relevant to the proper orientation of a neurophysiologist in his problems there cannot be less than 12 papers a day."[1] The psychiatric research worker trying to keep up to date with all the relevant literature therefore has an enormous task, and any opportunity to take stock must seem to him particularly welcome.

Such an opportunity was most agreeably given at the important conference held at Magdalen College, Oxford, last week. It was organized by the Research Committee of the Mental Health Research Fund, being its first project. The Fund, the purpose of which is "to promote, finance, and encourage research on mental health and disease," came into being in 1949, a very tangible sign of the growing pressure of public opinion that more should be done to prevent mental ill-health—which in terms of money alone probably costs about £100m. per year. It is all to the good, therefore, that laymen and women have joined with medical men and women to administer the Fund and to consider what the aims of mental-health research should be. In fact the Research Committee of the Fund has a lay chairman, Sir Geoffrey Vickers, V.C., who also most successfully took the chair at the Oxford conference, undeterred by the abstruse and highly technical nature of some of the discussions. A certain uneasiness about the language of psychiatry was apparent. As Professor MacCalman observed, the uninitiated show justifiable irritation when they find common words being given special meanings.

The terms of reference for the Conference were wide: "What are the ignorances which to-day principally hamper our understanding of the nature, prevention, and cure of mental illness? What advances

[1] Bates, J., in a paper presented to the Conference.
[2] The *Proceedings* of the Conference will be published this autumn by Blackwell Scientific Publications, Ltd., Oxford.

in research are most likely to remove these and so help to reduce the population of mental hospitals and institutions for delinquents?" Among those who discussed these questions were anatomists, physiologists, neurologists, neurosurgeons, neuropathologists, psychiatrists, psychologists, biochemists, pharmacologists, enzymologists, and sociologists. Broadly speaking, the psychiatrists were inclined to dwell on the enormous gaps in knowledge. Dr. Eliot Slater, for instance, remarked that psychiatry is nearly all "ignorance," and Professor MacCalman, in the opening address, emphasized that there was not yet any commonly agreed broad formulation of aetiological principles in psychiatric illness. Dr. Ström Olsen also spoke of our ignorance of the fundamental physiological and neuropathological processes in the brain, and Professor Aubrey Lewis of the neglect in this country of the vital statistics of mental illness, adding that little information is available about the history of patients with various mental disorders after they have ceased to be under medical care. The specialist research workers, on the other hand, justifiably enthusiastic about their new instruments and techniques (Professor A. Kennedy suggested that we were now in the golden age of methods and instruments), were able to show how the results of their investigations were leading to new concepts of mental health and to efforts to relate human and animal behaviour with biochemical and electrophysiological findings.

In anatomical studies designed to throw light on brain function, the so-called primitive elements in the human brain have until recently been neglected. But, as Professor Le Gros Clark told the Conference, these regions of the brain, which include the hypothalamus, are now known to be closely associated with emotional reactions of one sort or another, and further detailed research on the thalamic-reticular system should be rewarding. Dr. G. W. Harris, speaking of the nervous control of the secretions of the pituitary gland, mentioned the effects of emotional stimuli, and suggested that there might be a place for the localized application of electric stimuli to the hypothalamic region in certain psychotic patients. The forging of a link between neuro-anatomy and neurophysiology on the one hand and psycho-analysis on the other was mentioned hopefully by Dr. John Bowlby, who pleaded for neuro-anatomical studies on very young children and referred to the fact well known in embryology that the growth of cells is influenced by the particular environment in which they are at a particular phase of development. Dr. Bowlby also showed how studies of animal behaviour can throw light on man's social responses, whether normal or abnormal. It remains to be seen whether it will be possible to detect physical changes in the central nervous system when social responses go awry. But, as Dr. D. Richter reminded the Conference, the invention of new tools of research must not lead us to expect too much from the chemical and physical approaches towards the solution of psychiatric problems.

Much was said at the Conference about animal experiments, Professor R. W. Russell giving an illuminating account of experimental neurosis, but some doubt was expressed about the significance of these experiments to human behaviour—Professor Sandford, of Berkeley, California, asking the very pertinent question: What is the *normal* reaction of animals submitted to stressful situations? It was generally agreed that in the end experiments of this sort would have to be tried out on human subjects.

Many suggestions were made at the Conference about future research. There was strong support for Professor Aubrey Lewis's statement that research on the family must continue to be of prime interest. Professor T. S. Simey suggested that relationships between certain sorts of behaviour and certain sorts of family structure should be investigated, and Dr. J. M. Tanner, the honorary secretary of the Fund's research committee, pointed out how valuable would be the help of general practitioners in research on the behaviour and physiology of families. Supporting this, Professor Kennedy said there was still a need for kindly research—research in practical means of being kind to patients. In most of the fields of research into mental disorders there is no lack of material, but the neuropathologists complain of one serious shortage—brains from patients who have recovered from leucotomy and similar operations. The importance of these brains to research is obvious, and with the co-operation of general pathologists it should be possible for neuropathologists to examine many more of them than they do at present.

In an admirable and eloquent speech at the end of this encouraging and stimulating Conference[3] Sir David Henderson said it was still of the first importance to improve the status of psychiatry in the eyes of the medical profession as a whole. Fifty years ago the outlook of psychiatry was bounded by the wall of the mental hospital, but now psychiatry was entering a new era of activity—a fact which was plain to all those fortunate enough to attend the Conference. The object of research is no longer limited to finding new methods of diagnosis and treatment: the high ideal that can now be set is, as Sir David put it, to improve man in his social setting and so to obtain a saner world.

HEALTH SERVICE ESTIMATES

Once again the financial limit on the cost of the Health Service has been maintained. The estimates for 1952–3 published at the end of last week show a total net cost to the taxpayer of £402.3m., but the limit of £400m. imposed by three successive Chancellors has not in fact been exceeded. The cost of the Health Service as such has been kept down to £392m., compared with £398m. in the year just ending. The balance of £10m. is accounted for by civil defence.

The rise in prices in the last 12 months has been much greater than in the previous year. If allowance is made for this the cost of the Health Service has actually been reduced by a much greater amount than £6m. But the reduction is being imposed mainly by new raids on the patient's purse rather than by cutting the budgets of the various branches of the Health Service. Thus, instead of £392m., the estimated cost of the Health Service would have risen to about £420m. in the coming financial year had it not been for the savings effected by the proposed charges.

The prescriptions charge is estimated to bring in £7½m., and the charge for dental treatment, including the existing charge for dentures, about £11m. The existing charge for spectacles is estimated to bring in nearly £5. This, incidentally, is only slightly higher than the estimated receipts in the present financial year, when the charge was in force for only nine months.

It has been said that the introduction of a charge had a deterrent effect on the demand for spectacles, and the new estimates of the cost of the supplementary ophthalmic service seem to bear this view out. In any case, demand was falling from the high levels of the first two years of the Service. The gross estimate is now only £11m., compared with about £28m. in 1950–1. Unfortunately this is not true of the pharmaceutical service, the cost of which according to Mr. Crookshank is at the moment running at the rate of over £50m. a year. Here again the charge will probably act as a deterrent, for the estimates show a gross cost, before allowing for the proposed charge, of £47½m.

By keeping the net total cost of the Health Service down to £392m. Mr. Butler has a slightly bigger margin in hand than Mr. Gaitskell a year ago. On the other hand, the Bill introducing the new charges has been considerably delayed, and will now not come into force as soon as had been intended when the estimates were drawn up. This means that the receipts from the charges will be less than these estimates. It has also been reported that during the delay the Bill has been modified and further exemptions from the charges proposed. As the Bill was due to have its Second Reading on Thursday after we had gone to press, these reports have presumably been confirmed or denied, and if true the effect on the estimates explained.

In any case, slightly bigger as this year's margin is, it still leaves very little balance if prices continue to rise as rapidly as they have done. And the hospitals, which have come off best in the new estimates by obtaining an increase of about £20m. in their budgets, are nevertheless far from satisfied. In a time of rising prices they are hard put to it to maintain their existing services, much less expand them. Inflation hits them in the higher prices for food, fuel and power, drugs, and equipment, and in the increases that may be granted in wages and salaries to offset the higher cost of living.

How long can the uneasy financial stability of the Health Service continue? If prices continue to rise, can the Chancellor repeat his policy of allowing the Service roughly the same amount of resources at the new prices by imposing more, or heavier, charges on patients? The proposed charges are unpopular, and it will not be easy for him to maintain the hospitals by mulcting still further the patients who need a bottle of medicine or dental treatment.

On the other hand, if he does not do this, he will have to spread the burden of the higher financial cost on the general body of taxpayers; and heavier taxation would be contrary to the policy proclaimed in this year's Budget of restoring incentives to harder work and higher output. Nor would taxation be such an efficient method of paying for the higher cost of the Service, since the deterrent effect would be absent. The choice is not easy; and it appears that until inflation is checked the finances of the Health Service, though under control, will still be precariously balanced from year to year.

THE NATIONAL FORMULARY AND "PRESCRIBERS' NOTES"

The 1952 edition of the *National Formulary* is now published, and, for the purposes of the National Health Service, will take the place of the 1949 *Formulary* from June 1. All doctors and pharmaceutical chemists participating in the Service will shortly be supplied with a copy. The Joint Formulary Committee, appointed by the medical and pharmaceutical professions under the chairmanship of Professor Wayne, has been responsible for the revision of the 1949 *Formulary* and has effected numerous improvements.

Freedom to prescribe what a doctor considers best for his patient has always been a jealously guarded prerogative of the medical profession, and many doctors have regarded official formularies with some suspicion as tending towards regimentation, and even direction, in prescribing. The issue of the *Formulary*, of course, in no way limits the prescriber to the preparations contained therein or to the form in which they are prescribed. There can be few occasions in practice, however, which demand the use of preparations not included in this work, even though it retains its pocket size, nor is it likely that the prescriptions of many doctors could compete with those in the *Formulary* in efficiency. Further, the general adoption of the preparations suggested would go far towards economizing on the national bill for drugs—a crucial necessity at the present time.

Twenty-seven pages are devoted to "Notes for Prescribers"; this was an acceptable feature of the 1949 *Formulary*, and it has been enlarged in the present one to include a number of new monographs. These compress a remarkable amount of essential information on therapeutics into a very small space. The practical, yet critical and scientific, approach to the problems discussed in these notes contrasts a little strangely with some of the preparations which appear later in the general section of the *Formulary*. For example, the scepticism shown in the "Notes for Prescribers" about the value of stimulant expectorants makes it surprising to find so many expectorant preparations among the mixtures listed. It would be inconceivable, however, for any formulary to satisfy completely all its medical users. There will be those who will consider that the committee has not been sufficiently drastic in deleting from the *Formulary* certain drugs believed to have had their day and been found wanting—such as bromides, potassium chlorate, colocynth, and jalap—while others will nostalgically regret the disappearance of grey powder, A.B.C. liniment, and creosote. On the whole the committee must be congratulated on having steered a safe course between the Scylla of scientific nihilism on the one hand and the Charybdis of reactionary empiricism on the other.

The compilers of the *Formulary* have given much thought to making the mixtures for infants more palatable. There are difficulties in getting a wide range of fruit flavours for mixtures and linctuses, because no standards exist for most of the commercial fruit flavours, but good use has been made of syrup of raspberry, and, to a less extent, of syrup of blackcurrant, for which standards are available.

Another important innovation is the introduction of English headings for the subsections of the *Formulary*, which leads to a more rational grouping—for example, eye drops, eye lotions, and eye ointments now occur together, whereas guttae, collyria, and oculenta were widely separated in the first edition. Coming events cast their shadows before, and the day may not now be far distant when the dog Latin of prescribing may be dropped altogether. However much we might regret such a change on sentimental grounds, it must be realized that Latin is no longer the common language of scholars—far less of doctors—and that its continued use in prescribing has far more disadvantages than advantages. No benefit is gained by adding the suffix "um" to the name of new drugs, and the difficulty of giving them Latin titles is well illustrated by Injectio Procainae Benzylpenicillini Confirmata. Indeed, these difficulties have already proved insurmountable in the monographs devoted to "Preparations of Human Blood" in the *Addendum* to the *B.P.* in 1948. Apparently no member of the Pharmacopoeia Commission was sufficiently versed in the humanities to turn "Concentrated Human Red Blood Corpuscles" into Latin.

Another aid to prescribing has appeared this week. Under the title "Prescribers' Notes" the Ministry of Health and the Department of Health for Scotland are issuing to all N.H.S. doctors a loose-leaf folder giving information on the use and cost of drugs and dressings. The first number begins by pointing out that the estimated cost of the general pharmaceutical services in Britain in 1951–2 was over 20s. a head. The purpose of the notes is to offer examples of prescriptions "which might have been more economically done if information such as is included in these notes had been available to the doctor concerned." But there is no intention of interfering with the doctor's treatment of his cases. A week's treatment with chloramphenicol is shown to cost about £11, while treatment for about the same time with sulphonamides or penicillin costs about 10s. The indications for and against using chloramphenicol are listed.

The notes draw attention to the possibilities of using smaller packs of various dressings than are sometimes prescribed, and cellulose tissue is said to be cheaper than absorbent cotton-wool by 4s. 1½d. per lb. Figures at the end show that in 1950 18% of all prescriptions in the N.H.S. in England and Wales were for proprietary preparations, while in Scotland the proportion was 26%. The proportionate cost of ingredients in England and Wales was 44%, and in Scotland 47%. The notes are designed for filing in an ordinary record cabinet. They have been compiled with the guidance of nominees of the General Medical Services Committee.

CHEMOTHERAPY, ALLERGY, AND TUBERCULOSIS

The general question whether allergy to bacteria or their products is a reaction useful to immunity or merely an unfortunate side-effect of certain types of infection has divided immunologists for years. The subject has been critically reviewed by Hadfield and Garrod,[1] who consider that the weight of evidence favours the latter view. This is evidently the opinion of Long and

[1] *Recent Advances in Pathology*, 1947, London.
[2] *British Medical Journal*, 1951, **2**, 37.
[3] Long, D. A., *Bull. schweiz. Akad. med. Wiss.*, 1952, **8**, 194.
[4] Cornforth, J. W., Hart, P. D'Arcy, Rees, R. J. W., and Stock, J. A. *Nature, Lond.*, 1951, **168**, 150.
[5] Hart, P. D'Arcy, and Rees, R. J. W., *Lancet*, 1950, **2**, 391.
[6] Ibid., 1951, **2**, 522.

his colleagues at the National Institute for Medical Research, since their work, to which we have referred in these columns[2] and which has recently been recapitulated in a single paper,[3] is based on the assumption that rheumatic fever is essentially due to a hypersensitivity reaction to streptococcal allergens, analogous to tuberculin hypersensitivity. In an attempt to elucidate the pathology of rheumatic fever, they studied the sensitivity of guinea-pig skin to tuberculin and the effect upon it of mild ascorbic-acid deficiency, and of treatment with thyroxine, A.C.T.H., and cortisone. It is suggested, on the basis of such experiments, that the action of cortisone in the tissues of guinea-pigs sensitized by injections of B.C.G. is to facilitate the oxidation of ascorbic acid to dehydroascorbic acid, a process associated with a diminution in sensitivity to tuberculin, linked with sulphydryl metabolism, and requiring thyroxine.

The theoretical justification for such an approach might be disputed and the analogy to rheumatic disease prove unacceptable, but the use of these methods to investigate the mode of action of antituberculous agents upon experimental tuberculosis in guinea-pigs needs no defence. Elsewhere in this issue, Drs. P. D'Arcy Hart, D. A. Long, and R. J. W. Rees show that the polyoxyethylene ethers (a group of detergents used commercially in the United States), previously shown to exercise an antituberculous effect in mice,[4] exert a similar effect in guinea-pigs—an effect which in the latter species is invariably associated with diminished sensitivity to tuberculin. This desensitization is comparable in degree to that of cortisone, but differs from it in being independent of dietary and hormonal factors. Attempts to explain the antituberculous effect in terms of antibacterial action, increased phagocytosis, or exaggerated antibody response proved unsuccessful. The chief stumbling-block to attributing the antituberculous effect of these drugs to their desensitizing power is that cortisone, with its comparable desensitizing power, has proved pro-tuberculous, at least in mice.[5] It is suggested that cortisone may differ from the detergents by depressing the mesenchymal cellular immune response to tuberculosis, and that this outweighs the benefits of desensitization; such an interpretation is in keeping with the facts, but must remain hypothetical until further studies elucidate the problem.

Fortunately other desensitizing agents are at hand. Fisher, Harington, and Long,[6] have recently shown that the action of N-acetylsphingosine in causing a diminution in sensitivity to tuberculin resembles that of these detergents. Dehydroascorbic acid and alloxan also possess comparable desensitizing power.[3] Hart and his colleagues intend to test these compounds for antituberculous activity, which, if proved, would strengthen the hypothesis of a causal connexion between desensitization and chemotherapeutic activity. Whatever the outcome of these experiments, the introduction of this group of antituberculous and desensitizing agents has provided a new approach to an important subject, and with it the idea of a chemotherapeutic agent exerting its effect, not upon the tubercle bacillus, but upon the host.

FELLOWS OF THE ROYAL SOCIETY

Three medical men and one medical woman were among the new Fellows of the Royal Society elected on March 20—Professor Bernhard Katz, Professor J. S. Mitchell, Dr. R. R. Race, and Dr. Marthe Louise Vogt.

Professor Katz is distinguished for his contributions to neurophysiology, and particularly for his work on nervous impulses and muscle end-plate potentials. He is at present professor of biophysics at University College, London. He graduated in medicine at the University of Leipzig in 1934. After holding a Beit Memorial Research Fellowship at University College he went as a Carnegie Research Fellow to Sydney, where he was also honorary lecturer in physiology at the University. He returned to University College, London, in 1946 as an honorary research associate and Henry Head Research Fellow of the Royal Society. Professor Mitchell has been professor of radiotherapeutics in the University of Cambridge since 1946, when this chair was established. He is also director of the radiotherapeutic centre at Addenbrooke's Hospital. Graduating in medicine in 1934, he was elected a Fellow of St. John's College two years later. Professor Mitchell's contributions to knowledge about the mechanism of the therapeutic action of radiations have been of outstanding importance. He was appointed C.B.E. last June. Dr. R. R. Race is the director of the Medical Research Council's Blood Group Research Unit at the Lister Institute. Qualifying in medicine in 1933, he was at one time assistant serologist at the Galton Laboratory, University College. His work on the rhesus and other factors capable of causing haemolytic disease has helped to complete one of the most remarkable of recent medical advances. Dr. Marthe Vogt has been lecturer in pharmacology in the University of Edinburgh since 1947. She graduated in medicine at the University of Berlin in 1928, and is well known for her work on the regulation of the secretion of the cortical hormones of the suprarenal gland.

Some of the other newly elected Fellows of the Royal Society have made important contributions to medical science. Dr. Honor Fell, who is Foulerton Research Fellow of the Royal Society and director of the Strangeways Research Laboratory, Cambridge, has greatly advanced the study of living tissues, particularly the mechanisms governing cartilage and bone formation. She is one of the editors of *Experimental Cell Research*. Dr. Rudolf Lemberg is director of the biochemical department of the Institute of Medical Research, Royal North Shore Hospital, Sydney. He has published many papers on the subject of metabolism of pigments derived from haemoglobin. Dr. D. D. Woods, reader in microbiology at Oxford University, played a major part in working out the explanation of the antibacterial action of the sulphonamides and has made many important contributions to bacterial chemistry.

We announce with regret the death on March 21, at the age of 79, of Professor Edwin Bramwell, formerly professor of clinical medicine in the University of Edinburgh.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

EMPYEMA

BY

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Many pneumonias are cured by antibiotics; the more pneumonias cured, the fewer the empyemas. This accounts for the considerable reduction in the frequency of pleural infection at the present time as compared with, say, eight or ten years ago. Nevertheless, the distressing picture of an established chronic empyema, with toxaemia, loss of lung function, and a deformed chest, should always be kept in mind as a warning of what may happen if the early stages are not recognized, or are improperly treated.

Pathology

Infection of the pleural cavity is commonly secondary to inflammation of the underlying lung. There are other causes, such as penetrating wounds, which must include the incautious use of the aspiration needle in search of a subphrenic abscess, but for practical purposes the lung can be regarded as the primary focus. Tuberculous empyema should be regarded as a separate problem.

The earliest stage of pleural inflammation is the formation of an exudate, usually clear and containing bacteria, but rapidly becoming turbid as the cellular content of the fluid increases. This stage is conveniently referred to as "diffuse suppurative pleurisy," since, in the absence of pleural adhesions, the whole cavity is potentially infected. The characteristic shape of the effusion is the result of gravity opposed by the subatmospheric pressure of the pleural cavity; the usual basal position can be altered by changing the patient's position. The lung is collapsed and pushed aside as the fluid collects, and if a large volume accumulates the mediastinum will be displaced. The amount of fibrin in the effusion varies with different organisms; it is small with streptococcal infections, which are slow to localize, and is much more massive in the presence of the pneumococcus. Within a few days of onset the fluid is frankly purulent and fibrin is being deposited on the chest wall and over the lung surface; flakes, and even masses, of fibrin float loose in the effusion. At this stage lung and chest wall become adherent at the margins of the fluid and a "localized pleural abscess" can be said to be forming. An abscess with appreciable walls develops in 10 to 14 days, and if not treated the fibrin walls become firmly organized and rigid, progressively binding down the lung and preventing the chest wall from moving. This fibrin capsule is three or four times as thick over the chest wall as over the lung surface.

Diagnosis

The early signs of fluid over a consolidated lung are not always easy to make out. Dullness is more marked and breath sounds are more distant or absent with aegophony towards the thin margins of the fluid, but it is often difficult to be certain that a thin layer of fluid is or is not present when the signs in the lung are still well marked. This applies particularly to children. Later, increasing loss of movement and absence of air entry make the diagnosis more certain, and radiology can give considerable help so long as the film taken is a good one. Too often the use of indifferent or portable apparatus fails to give the necessary help. There is only one certain method of diagnosis: that is, aspiration of infected fluid.

The diagnosis should be easily established when there is enough fluid to produce pressure on the mediastinum. In such cases marked shortness of breath and even cyanosis are added to the clinical signs, which include shifting of the apex beat and angulation of the trachea from the midline in the suprasternal notch.

Principles of Treatment

The principles that underlie treatment are twofold: (1) the toxaemic element must be eliminated and the products of inflammation moved from the pleural cavity, and (2) the lung must be re-expanded at the earliest possible moment, before it has become pinned down by fibrous tissue. This second factor is too often lost sight of because in other parts of the body drainage of an abscess (in the pelvis, for example) is followed by spontaneous obliteration of the cavity as the soft walls come together. In the thorax, however, the rigid chest wall and the collapse of the lung produce a firm-walled space which, if not treated correctly, may persist.

Treatment starts from the moment the diagnosis is made certain. Aspiration not only proves the presence of fluid or pus, but enables bacteriological examination to be carried out. In the early stages, as has been indicated, during the process of diffuse suppuration the fluid may be thin and almost clear even though loaded with organisms, but more commonly by the time aspiration is initiated frank pus will have formed. When the nature of the fluid and its bacteriological character have been established energetic measures should be undertaken without delay to empty the pleural cavity.

Aspiration

Drainage and aspiration should not be looked upon as separate procedures. Aspiration is the equivalent of intermittent drainage, and if it is carried out properly it is of inestimable value, since it removes pleural fluid by a closed system—that is, one which does not admit air from outside. Unfortunately it is often used perfunctorily and inadequately, with unfortunate results on the course of the empyema.

Thorough aspiration may take a considerable time and must be performed with a needle of adequate size fitted with a two-way tap to a large syringe. The habit of using an ordinary 10-ml. syringe with an ordinary needle is fraught with potential danger because disconnexion from the syringe may allow air to seep into the space, and if the empyema is not firmly localized the bubble of air will rise to the top of the chest and allow the lung to fall away from the apex. In other words, a collection of a small amount of fluid in the base of the chest may be turned into a pyopneumothorax with a fluid level and a collapsed lung. A localized empyema is converted into a total pleural infection.

Martin's syringe and needles make a convenient form of apparatus, consisting of a 20-ml. Luer syringe fitted to a two-way tap and with lock fittings to prevent accidental disconnexion. A selection of needles is required, and though a wide-bore needle may be needed if the pus is thick a fairly fine needle can be used for a start. The whole apparatus should be tested for patency and for absence of leak before the operation.

The patient sits up in bed and leans over a pile of pillows or a bed table; he may be even more comfortable sitting sideways with the legs over the edge of the bed. A preliminary sedative is an advantage in most cases. The skin is cleaned over the site, which has been previously determined by percussion and radiology, and is usually about four fingerbreadths from the midline posteriorly in the

eighth or ninth space (if the twelfth rib is difficult to palpate it is useful to remember that the scapula lies over the seventh space). A wheal of local analgesic is produced in the skin, and 5–7 ml. of the analgesic is injected into the chest-wall tissues, particularly into the immediately subpleural layer. If a wide needle is being used a tiny incision through skin only, made with a tenotomy knife, makes the introduction of the needle easier. Some fluid—for example, local analgesic—should always be present in the aspirating syringe to prevent bursting of the barrel if the piston flies back suddenly on being released.

Aspiration must be as complete as possible, and the operation may take 20 to 30 minutes. If fluid is removed too quickly the patient will feel uncomfortable and develop bouts of coughing, but if the procedure is carried out slowly and, above all, with the needle rigidly still the contents will be evacuated and the lung at the same time encouraged to re-expand. If bacteriology is indefinite, as may well be the case if antibiotics have been used, aspiration must still be performed in just as complete a manner. If, on the other hand, there are active organisms in the fluid an injection of the appropriate antibiotic should follow. Penicillin is the usual agent, and 500,000 units in 10 ml. of saline can be introduced at the end of the aspiration.

The next important step is to ensure that further complete aspirations are carried out as often as any fluid collects; and this does not mean that one should wait three to four days, or even longer, to see what is going to happen. If treatment is to be effective the pleural cavity must be emptied, if necessary, on consecutive days, and aspiration should be abandoned only if the fluid becomes too thick to flow through the needle or, as more commonly happens, flakes of fibrin obstruct the flow. This is probably the most important point in treatment, and one which is often found at the first aspiration. When this occurs it can safely be assumed that the pus is localized, and indeed the thickening of the pleura may be easily obvious on *x*-ray examination or felt during the passage of the aspirating needle.

Surgical Drainage

When aspiration has become impracticable the decision on the next move depends on the bacteriological findings. If there are still active organisms the abscess should be drained by rib resection at the lowest possible point, accompanied by thorough toilet of the inside of the cavity and wide-tube drainage.

The operation can be carried out under local or general anaesthesia. The patient should be in the sitting position in order to avoid the formidable risk of pus pouring into the lung through an unsuspected broncho-pleural fistula. The lowest point of the cavity is determined by previous aspiration or, in cases of difficulty, after study of two-plane radiographs following injection of 10–15 ml. of radio-opaque oil into the cavity. A vertical skin incision is made. The usual site is the ninth rib, 2 to 4 in. (5 to 10 cm.) from the midline, closer to the spine than might be expected. The rib is stripped of periosteum before removing 2 to 3 in. (5 to 7.5 cm.) of its length, and complete haemostasis obtained before the pleura is opened. A piece of pleura is routinely taken for section to exclude tuberculosis, neoplasm, and so on, and, after the pus and fibrin masses have been removed, the interior of the empyema is inspected and freed from all loose tissue. A wide tube is then inserted: the tube must be placed so as to avoid intercostal vessels and nerves, with its interior opening inside the empyema but not so far as to impinge on lung. Its distal end should not project more than a few millimetres beyond the skin—merely enough, in other words, to hold a safety-pin which, in turn, is attached to the skin by pieces of adhesive plaster. The tube is covered with a simple dressing held in place by a "corset" of strapping, which avoids the discomfort of bulky dressings so common in the past.

The control of drainage tubes is the surgeon's problem, and not one to be left casually to students or nurses. When a tube is used a number of common errors must be guarded against. In the first place the tube may not be large enough; if the tube is not placed at the bottom of the cavity, drainage will be incomplete. If the tube is changed frequently the contracting skin incision will sooner or later necessitate a smaller tube, and if this happens more than once or twice the drainage opening may become completely inadequate. Many cases of comparatively large chronic empyemas with pin-point sinuses intermittently discharging quantities of pus have been seen in the past. The time for removal of the drainage tube can be summarized by saying that the *tube is never removed from the pleural space but only from a track in the chest wall.* In other words, internal healing must be confirmed by pleurograms (two-plane radiographs taken after filling the space with radio-opaque oil) at 10- to 14-day intervals until the space is finally obliterated.

Breathing Exercises

Even with the most efficient treatment by drugs and surgery the result will be valueless unless at the same time the collapsed lung expands again. The lung must be induced to re-expand, not only to obliterate the empyema space, but to restore pulmonary function. Left to his own inclinations the patient will not move the affected part of the chest more than he can help; the instinct is to immobilize the area. But recovery is complete only when the chest walls are moving freely, and for practical purposes the movement of the chest wall is an index of lung expansion and function. A flattened rigid chest wall is almost certain to conceal an inactive area of lung.

The answer lies in the concentrated application of special breathing exercises which aim at producing a powerful and localized inspiratory excursion over the damaged area. Expiratory exercises, represented by puffing and blowing, should be ignored. The patient is instructed to breathe in deeply and forcibly against the light pressure of the physiotherapist's hand without arching or bowing the spine. After a few days he should be able to concentrate the effort in any part of the chest and he must then practise without fail for 10 to 15 minutes every waking hour, with a check once or twice a day by the physiotherapist. It is the conscientious patient who benefits and reduces his convalescence to a minimum.

The actual exercises are quite simple, but one must repeat that it is persistence and concentration that count. They are begun almost from the day of diagnosis and are continued with increasing intensity until complete recovery results, with the bad side of the chest moving even better than the normal side. The activities of the patient are encouraged by having him ambulant as soon as the grosser signs of toxaemia have been eliminated. The practice of keeping a patient in bed during the whole period of aspiration or drainage is detrimental to early recovery. During the final stages of closure of the empyema patients benefit by active exercise, and many of our patients are walking 8 to 10 miles (12.9 to 16 km.) a day as part of their convalescent treatment.

The Sterile Empyema

A difficult decision on treatment arises when a sterile empyema is encountered. The fluid has been sterilized by the action of penicillin, and the problem is that of a sterile abscess with thick fibrin walls. This poses the question of differentiating this form of empyema from one of tuberculous origin in which, in the absence of acid-fast organisms, a high proportion of lymphocytes in the pus may be the only clue, apart from the clinical history. A sterilized pyogenic abscess usually contains numerous broken-down polymorphonuclear leucocytes, and the shadowy forms of dead bacteria may be seen though bacteriological culture remains sterile. Indeed, a smear film often gives more satisfactory and certainly quicker information in all stages of pleural infection. The fibrin deposit in sterile cases is

even thicker than usual, because with the destruction of bacteria fibrinolytic enzymes are also destroyed. These enzymes are actually manufactured, under the names of "streptokinase" and "streptodornase," and can be introduced with the object of dissolving fibrin. There is a natural reluctance to drain a sterile cavity, with the result that many of these "penicillin empyemas" are left alone, and the thick walls of the persistent cavity prevent healing. Nearly all these cases can be attributed to faulty handling in the form of tardy diagnosis or inadequate aspiration.

In some cases breathing exercises and proper aspiration will start the closure of the cavity, but some do not respond because of the thickness of the contents, as well as the rigidity of the walls, and here two courses of action are open. The cavity can be opened and evacuated through a rib-resection incision, but drainage is not used; instead the skin only is sutured and breathing exercises are intensified. If this fails it is a simple matter to open the skin and insert a drainage tube. The second more radical and severe operation is that of decortication or pleurectomy, which in its best form entails complete excision of the empyema through a thoracotomy incision. The parietal pleura is removed from the chest wall and the lung is freed from its casing. Closed suction drainage and active physiotherapy encourage re-expansion of the lung and obliteration of the dead space. Pleurectomy should not be undertaken for at least six to eight weeks from the onset, and then only if other methods have failed. It can produce excellent results, but it is an operation of some severity and should not be performed if improvement is occurring under more simple measures. Where there is efficient physiotherapy it is not often indicated.

Prognosis

A properly treated empyema of moderate size and severity should be cured in 8 to 10 weeks at the outside. Beyond this period cavity healing is slow and the empyema is well on the way to becoming chronic. A chronic empyema is a formidable disability which may take months to cure, and a useful aphorism to remember is "a week's delay in the early stages means a month's longer convalescence."

Common Causes of Delayed Resolution

There are still many errors in treatment that could be remedied. In the first place diagnosis is not always made early enough, and thoracic surgeons commonly see cases of empyema which are at least a month or six weeks old and which have not been previously treated. Sometimes a collection of fluid that is awkwardly placed may be responsible for the failure to recognize the condition, but usually it is because the lung signs have dominated the picture and the question of pleural infection has been ignored. There may have been failure to start treatment even when the condition has been suspected. Diagnostic aspiration may be put off for a day or so and complete aspiration may be delayed for two or three days while awaiting bacteriological reports and so on. Even when aspiration has been carried out there is sometimes no attempt at any further aspiration, even though the fluid re-collects. Aspiration is often suspended because the pus is sterile. The formal aspiration itself may fail because of faulty apparatus or obstruction of the needle by fibrin flakes. Admission of air is a danger already mentioned. Frequently, once 200 to 300 ml. has been withdrawn, the patient or operator tires and the evacuation of fluid is incomplete. Again, there is too often marked delay between the aspirations and the failure to recognize that complete removal of the fluid will help the re-expansion of the lung. Too much dependence is placed on antibiotics, particularly if these have resolved the infection and signs of toxaemia in the patient. There is also a tendency to delay consultation with the surgeon until some days after aspiration has started to be difficult. There should be complete continuity in the treatment from the original recognition of fluid until the space is completely and finally obliterated.

There are atypical forms of empyema which are admittedly difficult to diagnose and treat. The discussion has been concerned so far with a limited collection of pus at the bottom of the chest, but the infection can be total or localized to some unusual site. A total empyema requires the most energetic and early treatment if the lung is to re-expand readily, and suction drainage or continuous aspiration can be used with advantage before too much fibrin has been deposited. The lung expands more readily at the base, and may shut off an apical pocket which requires individual treatment. Interlobar collections are more usually placed anteriorly and can easily be missed if good lateral radiographs are omitted. The same applies to pockets placed well above the diaphragm. Mediastinal empyema, which is often mentioned in textbooks, is very rare.

The differentiation between basal empyema and subphrenic abscess, lung abscess, and infected cysts is difficult, particularly if the empyema is complicated by a bronchopleural fistula. An empyema may heal spontaneously by rupturing through the chest wall or into a lung, but the dangers of the latter range from immediate drowning to chronic pulmonary infection. When empyema is secondary to carcinoma of lung it is possible that it may not heal, and the same applies if a tuberculous infection of the pleura is present. An actinomycotic empyema may heal, but will persist if the lung disease is progressive.

There are few examples in medicine in which early and prompt treatment can pay such dividends as in pleural infection. Antibiotics have reduced its incidence, but diagnosis and treatment have not kept pace, with the result that the spectre of chronic empyema still remains to be finally exorcized.

Next Refresher Course Article.—"The Psychiatric Case and the Law," by Professor Alexander Kennedy.

Nova et Vetera

PIONEERS OF ANAESTHESIA

The English Pioneers of Anaesthesia (Beddoes, Davy, and Hickman). By F. F. Cartwright. (Pp. 338; 20 figures. 21s.) Bristol: John Wright and Sons, 1952.

Dr. Cartwright has told us much of the lives of three men of extremely different mentality, character, and fate. There results a valuable and instructive picture of the conditions of experimental investigation in the late eighteenth and early nineteenth centuries in England, where laboratories hardly existed. In the whole of Britain it was only at Edinburgh and Glasgow that scientific university training was available. Of the three men with whom the book is concerned, only Davy is generally remembered. Beddoes is known to a few, though rather for his associations than for himself, while Hickman is recalled only by a handful of historical specialists. Here Fame must be adjudged to have distributed her favours justly.

From the earliest times attempts have been made to procure unconsciousness during operations by drugs, both ingested and inhaled. "God caused a deep sleep to fall upon Adam, and He took one of his ribs and closed up the flesh thereof" (Genesis ii. 21).

> "I'll imitate the pities of old surgeons
> To this lost limb, who, ere they show their art,
> Cast one asleep, then cut the diseased part."
> (Thomas Middleton, *Women Beware Women*, *c.* 1620.)

Between the dates when these two passages were written, and indeed both before and after, this idea has been in the

minds of thousands of surgeons. The *spongia somnifera* was a commonplace of surgery for ages. Therefore, for having attempted to produce anaesthesia neither Beddoes, nor Davy, nor Hickman deserves any credit at all, and it is only by the means that they adopted that they can be judged. Nevertheless these men were so diverse in temperament and scientific approach that their consideration within the covers of one book gives special interest to Dr. Cartwright's narrative. For truly the psychology of discovery is an absorbing theme; it is a pattern not only intricate in itself but susceptible of endless variation.

Thomas Beddoes (1760–1808) was a member of a trading and farming family in Shropshire. He was educated at Oxford, took an interest in languages, and translated some important scientific works into English. He turned early to chemistry and geology. After a time at Edinburgh he took his M.D. in 1786, visited Paris, and in 1787 became reader in chemistry at Oxford. By temper restless and by opinion radical, he had no easy position in that conservative centre. After trying London and Birmingham, he settled in Bristol, where he started practice and a laboratory. In 1793 he founded an institute for "Pneumatic Medicine." It was the age of the "new chemistry" of Black, Lavoisier, and Priestley. "Gases"—by your leave—were in the air and were a general subject of scientific conversation. Beddoes had a real genius for intellectual friendship and absorbed much on gases—interpreting some of it wrongly and some of it even fantastically. He was bursting with ideas but was weak in designing experiments, far from strong in performing them, and persistent in misinterpreting them. He had no clear notion either of controls or of limitation of variables—the two sheet anchors of those who would embark on the experimental way. He was convinced, against the evidence, of the beneficial effect of inhaling "factitious airs"—that is, of the simpler gases that were then the subject of much investigation. He achieved nothing scientifically important, and his wayward genius turned to other fields. His institute rightly came to an end, but not before his perceptiveness of human qualities had distinguished the genius of his brilliant assistant, Humphry Davy. Dr. Cartwright's treatment of the intricate personality of Beddoes is a real addition to our knowledge of the scientific scene of the time.

Of Davy less need be said here, for so much more is known. Undoubtedly he is responsible for the effective knowledge and action of nitrous oxide and so, at some remove, for its use in surgery. His own many experiments with it, including many on himself, resulted in the phenomena which gave it the name of "laughing gas." He was not a doctor nor was he particularly physiologically minded, but he was, nevertheless, the effective founding father of modern anaesthesia.

Henry Hill Hickman (1800–30) is a peculiar and pathetic figure. He died untimely. It is impossible to say what a young man of 30, of an experimental disposition, might have done. Such young men are rare. What he did, in sober fact, was to show how *not* to anaesthetize. In a series of experiments on animals he used carbon dioxide as an inhalant. Unconsciousness ensued. It was then possible to remove a part without sign of pain. It was also possible, under experimental conditions, to revive the creature afterward, a fact long known from demonstrations to tourists at the "dog's grotto" near Naples. This scene had formed a high spot in the Grand Tour as organized for young sprigs of the nobility and gentry since the sixteenth century. Hickman showed persistence, experimental talent, enthusiasm, good faith, and good will. It is easy to see now that he was on the wrong line. Who shall say whether, given time, he would have had the flexibility and open-mindedness to shift to a more hopeful approach? It might have been. It might have been. A sad story well told. But it may not be generally known—it was not to the reviewer—that the late C. J. S. Thompson, of the Wellcome Historical Medical Museum, was a grandson of this unfortunate young man.

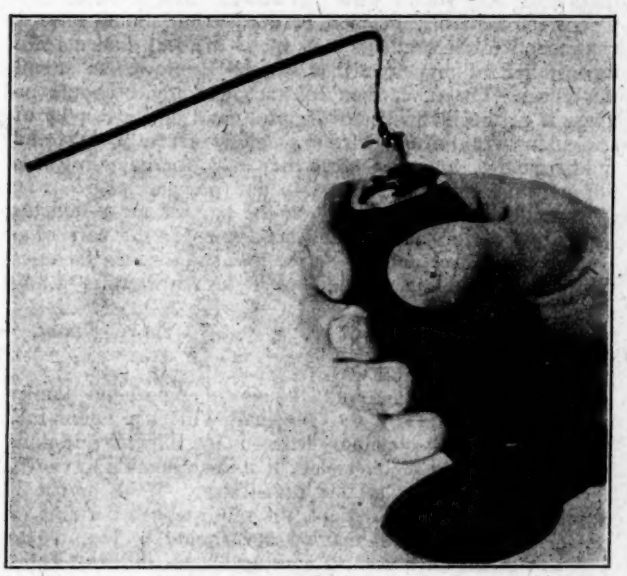
CHARLES SINGER.

Preparations and Appliances

AN AID TO ANALGESIA OF THE LARYNX AND TRACHEA

Dr. T. DINSDALE, anaesthetist, Manchester Royal Infirmary, writes: In 1949 I described a technique of topical analgesia for bronchoscopy. This involves three steps—namely, spraying the mouth and pharynx; swabbing the pyriform fossae; and injecting 2 ml. of analgesic solution through the cords, using a laryngoscope and a syringe with a cranked nozzle.

There have been many reports (Thomas and Fenton, 1943; Titche, 1947; Richards, 1947; Jackson, 1949; Weisel and Tella, 1951) of toxic reactions following the use of 2% amethocaine solution, but our experience with a 1% solution is that it is both effective and safe when used carefully. Nevertheless, when using such crude nebulization as is provided by the average throat spray and injecting a further 2 ml. of liquid directly into the trachea, it is easy to appreciate that a considerable quantity of amethocaine may be absorbed. I discussed this aspect of local analgesia with Mr. James Juby, of Messrs. A. C. King Ltd., and he has designed a spray which overcomes most of the difficulties. It consists of a one-piece bulb and base with a concentric anaesthetic container holding 3 ml. This can be operated with one hand. To it is attached any of the standard nebulizers—for example, Magill's, Rowbotham's, etc. In addition there is a straight nebulizer, with the same angle as Magill's endotracheal-tube-holding forceps, for spraying the glottis when using an orthodox laryngoscope (see illustration). It is long enough to be applied through the cords to the upper end of the trachea. The tip should not be curved for use with a Macintosh laryngoscope, as this latter advantage is then lost. The fine spray provided by these nebulizers allows a much smaller total quantity of solution to be used: 3 ml. of 1% amethocaine is quite enough, if the pyriform fossae are swabbed, to provide perfect analgesia down to the carina in the adult.



I must thank Mr. Juby for the excellence of his design and the high standard of workmanship. The spray, to be known as the "multicaine spray," is obtainable from Messrs. A. C. King Ltd., 27, Devonshire Street, London, W.1, and can be supplied with the nebulizer described above or with any other standard pattern.

REFERENCES

Dinsdale, T. (1949). *Brit. J. Anaesth.*, 21, 193.
Jackson, C. A. (1949). *British Medical Journal*, 1, 99.
Richards, R. (1947). *Ibid.*, 2, 51.
Thomas, J. W., and Fenton, M. M. (1943). *J. Allergy*, 14, 145.
Titche, L. L. (1947). *Dis. Chest*, 13, 452.
Weisel, W., and Tella, R. A. (1951). *J. Amer. med. Ass.*, 147, 218.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Family Planning

SIR,—The Family Planning Committee of the Medical Women's Federation is to be congratulated on its memorandum (March 15, p. 595). The recommendations are both timely and courageous, especially the final one "that advice on family planning should be available to women who require it on medical grounds, and also to women who ask for it for the purpose of family spacing. . . ."

No one would disagree with the suggested groups in the profession who should give this advice. But I would add that every maternity hospital or department should have a contraceptive clinic attached to it; if medical students are in obstetric training there they should be allowed to attend this clinic. The time when contraceptive advice should be given is at the first visit to the post-natal clinic, usually at the sixth week after delivery. Many recently delivered mothers begin to worry before they leave the lying-in wards about future marital relationship and pregnancy.

It should be an obligation on the part of those—doctor or midwife—who have been responsible for the care of a woman during her delivery to see that she is given facilities for receiving contraceptive advice if she wishes this.—I am, etc.,

London, W.C.1. W. C. W. NIXON.

SIR,—The interesting and thoughtful report on family planning produced by the Medical Women's Federation (March 15, p. 595) inevitably leaves many difficult questions still unsolved. In the first place it seems desirable to clarify the position of the Catholic practitioner. If he or she is holding a public appointment, the old-established ruling of the Ministry of Health that no one should be required to give advice on birth control contrary to his religious belief still holds good and presumably is applicable to all medical practitioners under the National Health Service. I take it that if a non-Catholic patient of a Catholic doctor required birth-control advice on *medical* grounds and is not satisfied to accept such methods as the Catholic doctor feels able to recommend (i.e., safe period and abstinence), she should be instructed to apply at the Town Hall, where she will be directed to a clinic or to a general practitioner willing to meet her needs. This could easily be organized.

The problem of the woman who desires contraceptive advice "for the purpose of spacing her family" raises much broader issues. If the very sensible recommendation of the report of the Medical Women's Federation is accepted and a fee is collected for this service, the patient can of course go to any doctor or clinic she prefers without causing administrative confusion. But there are aspects of this matter which affect all of us without distinction of religion. It would have been helpful if the report (which shows a sensitive social outlook) had included a word of warning about the dangers inherent in a general policy of "spacing." We all know that such demands vary from the tragic to the merely frivolous. It would be only too easy in organizing a comprehensive service to create a "climate of opinion" in which the postponement of childbirth to a convenient period became the expected thing, and as life becomes progressively harder the convenient time for the second or even the first child might never come. Parenthood without prolonged sacrifice is a dangerous myth which enthusiasts for family planning may unwittingly foster. It is surely worth discussing whether the medical profession is to drift into a position of handing out contraceptive advice on demand or to maintain that it has some responsibility for seeing that the patient (and the nation) is not being encouraged in a disastrous policy.—I am, etc.,

London, S.W.3. LETITIA FAIRFIELD.

Soviet Genetics

SIR,—One would not venture to accuse a reviewer of prejudice did he not confess to it himself. Professor S. C. Harland (March 1, p. 472), in reviewing *Soviet Genetics*, by Morton, ends by saying: "All books by Russians or about Russians are exasperating, and this one is no exception to the rule. Russian genetics may be described as a mixture of the blatantly fraudulent, the naive, the nationalistic, the obvious, and perhaps, in rare cases, the interesting and novel." It seems from the context of the review that the Russian cotton geneticists have achieved results somewhat different from those obtained by Professor Harland, a not unusual circumstance in the history of scientific research. But the book contains a great deal of information far more important than this, and surely it might have had some mention in the review, "exasperating" though it probably is to the reviewer.—I am, etc.,

London, W.C.2. F. WOOD JONES.

SIR,—Perhaps I can make my position a little clearer to Professor F. Wood Jones. First, the work now being put out in Russia violates all the agreed rules for the writing of scientific papers. The methodology is not described in such a way that the experiments can be repeated and the results verified. Conclusions are consequently drawn from the data, which the reader is not able to draw for himself. In rare cases when it has been possible to repeat Russian experiments the results have never been confirmed. Perhaps a few of the latest claims made by the Russians may be cited as causes of exasperation. In a recent paper Lysenko says that in 1949 200 rye grains were found in ears of wheat. These gave mostly rye plants. Mention is made of barley plants obtained from seed of the branching wheat. Finally, to work on biology in the Soviet Union you have to believe in the inheritance of acquired characters because the Party has made this doctrine official, and you have to agree with the designation of Mendel as a "reactionary cleric."

My prejudice is merely against shoddy work and slipshod hypotheses.—I am, etc.,

Manchester, 13. S. C. HARLAND.

Carcinoma of the Stomach

SIR,—I have read with interest Dr. C. P. Petch's letter (March 1, p. 492) on diagnosis of carcinoma of the stomach and his statement that he has seen seven patients dying of gastric carcinoma in the last four years, and that in each case early diagnosis had been missed by barium meal. Final diagnosis rested on laparotomy or necropsy, and he asks for more reliable means of confirming clinical suspicions.

May I suggest that clinical evidence is often not obtained with sufficient care, as I know from experience? I always take the patient's history myself, especially when dealing with hospital patients. Even if careful radiology fails there is often a reliable means—namely, gastroscopy—and laparotomy is definitely justified if clinical symptoms are strongly suggestive, and in the hands of a good physician and surgeon I would gladly avail myself of this if the occasion arose; and surely gastric secretion investigation is not obsolete.—I am, etc.,

London, W.1. G. E. VILVANDRE.

Addison's Disease and Pregnancy

SIR,—I was very interested in the medical memorandum on this subject by Dr. T. A. Richards (February 23, p. 421). I had a case recently of a woman aged 25 who had been treated for Addison's disease for seven years. I will not

enter into details of the case, except to say that throughout the later part of the antenatal period the woman stated she was better than she had been for years. Her maintenance dose of "eucortone" was 5 ml. daily intramuscularly. She had had a D.C.A. implant of 300 mg. in January, 1951. The baby weighed 7 lb. 12 oz. (3.5 kg.) at birth, was alive, and appeared normal in every way. Although the woman gave a history that she had had a crisis in 1947 when she had been in coma for four days, also a crisis in March, 1950 (coma for three days), she went through the pregnancy, labour, and puerperium without any crisis. I was grateful to Dr. G. E. F. Sutton for the supervision of her medical care.

Dr. Richards omitted to record the most recent review of 39 cases by Dr. Florence Brent, of Brooklyn (*Amer. J. Surg.*, 1950, **79**, 645). Of her 22 full-term pregnancies 12 patients developed crises after delivery and seven patients died. She believes that patients with Addison's disease are very susceptible to barbiturates and morphine, and sedation throughout labour should be kept at a minimum. An interesting point she recorded was that none of the patients in the series had developed toxaemia of pregnancy. Spontaneous delivery at term was followed by the best results.

The association of pregnancy with Addison's disease is possibly becoming more common with greater improvement in the medical care of the Addison's disease. But as long ago as 1922 Dr. Gilbert Fitzpatrick, of Chicago (*Surg. Gynec. Obstet.*, 1922, **35**, 72), reported a case and reviewed the reports of 11 such cases already published. It was he who stated that lactation should be forbidden, "as it renders the patient weaker." Dr. S. L. Simpson (*Proc. roy. Soc. Med.*, 1946, **39**, 511) recorded two successful pregnancies in a case of Addison's disease.—I am, etc.,

Bristol. G. GORDON LENNON.

Goat's Milk and Infantile Eczema

SIR,—I feel that it is worth drawing the attention of your readers to some recent experiments in the treatment of infantile eczema. This condition, which first appears when the child is being fed primarily on cow's milk, has been considered to be due to an allergic reaction, and some cases have responded to a diet which contains no cow's milk. A diet of this type is, however, difficult to arrange and may result in other undesirable symptoms.

Two years ago it was decided to substitute goat's milk for cow's milk in the diet of two babies undergoing treatment for infantile eczema at a Midland hospital. Within three days the inflammation round the eczema patches had subsided, and in 33 days all signs of eczema had disappeared. The treatment was extended to five more babies with equally good results. Attempts to return to a diet of cow's milk, pasteurized or unpasteurized, and to patent baby foods all resulted in fresh outbreaks of eczema within 48 hours. The treatment is now being extended to older children and adults, and the results are promising, but not yet conclusive, in these long-standing cases.

If eczema is an allergic condition it is probable that the protein fraction of goat's milk is an important factor in the cure; but it is also important to remember that the fat in goat's milk is in a much more finely divided condition than in cow's milk and so can be more easily assimilated.—I am, etc.,

Salcombe. PHYLLIS G. CROFT.

Pink Disease and Infections

SIR,—Dr. W. J. M. McLeod (March 15, p. 605) makes appropriate comment on two cases of pink disease, reported by Dr. A. S. Cook (February 16, p. 383), which appeared to respond satisfactorily to antibiotic (chloramphenicol) therapy. Dr. McLeod's case of pink disease developed pertussis, and after three weeks all symptoms of pink disease had disappeared; and this was before the advent of antibiotics. He was able to refer to a case of pink disease cured by measles.

Because of his express interest in a possible relationship between pink disease and the common infections of infancy may I refer him to a recent paper on mercury and pink disease (*Lancet*, March 1, 1952, p. 441) by Dr. A. Holzel and myself? We mention a fact that "five children with severe pink disease showed simultaneous recovery from an intercurrent infection and the acrodynia. The intervening illnesses were measles in three cases, chicken-pox, and tonsillitis."—I am, etc.,

Manchester, 19. THEODORE JAMES.

What Doctors Prescribe

SIR,—On reading the article by Professor D. M. Dunlop and others (February 9, p. 292) I was assailed by a strong sense of guilt. I felt that something had to be done about it, so, picking up the textbook of medical treatment of which he is joint editor, I opened it at the preface.

I noted with satisfaction that in this book "the number of drugs advised are considerably fewer than in some books of therapeutics." Thus encouraged, I turned to the section on respiratory diseases, as I was rather uneasy about a couple of proprietary expectorants I am in the habit of prescribing for some of my many chronic bronchitics. I was taken aback to discover that I had neglected to give gargles, sprays, vitamins, and iron for prevention. I am certain that I have neglected to ensure an adequate protein intake in some of my cases and had almost completely ignored mixed anti-catarrhal stock vaccines. My crime in ordering an effective proprietary seemed less heinous when I discovered that had I followed the book I should have had to employ an expectorant combined possibly with an antispasmodic, and "sedative drugs separately." Nor was I to forget inhalations of medicated steam, digitalis in certain cases, and the control of obesity in others—by diet alone, no doubt, to save on the dextro-amphetamine—still keeping up the patient's resistance without recourse to any more vitamins, I suppose.

Still, I have no doubt that in practice Professor Dunlop and his learned colleagues know just how to combine all the excellent advice one finds in the best textbooks, cheaply and efficiently. One only hopes that in the future as in the past some of the experts will actually join the ranks of general practitioners and see the work at first hand. Misunderstandings arise when people seek to understand our job by browsing over prescriptions.—I am, etc.,

Scarborough. DAVID MCGILL.

SIR,—Psyche, soma, and surroundings mix, and the result is old Mrs. Brown, and only her G.P. knows what works with her. The expert, with usually only one ingredient to experiment on, gets a different result. Both are right: the expert writes an article explaining the errors of the G.P., and so it has always been. The trouble now is that the State leaps to believe the one receiving the salary of an expert and comes blundering in on the more complex triad—poor old Mrs. Brown.

A lecturer of old said to my Year, "It is quite ridiculous to give a cough mixture containing an expectorant and a sedative. But, gentlemen, it works!" And that is our operative word.—I am, etc.,

Cromer. A. H. GREGSON.

Medical Treatment of Hypertension

SIR,—In your leading article (March 15, p. 587) appears the statement: "There is now little doubt that surgical treatment has materially lowered the fatality rate of hypertension." It is to be regretted that a section of your journal which usually carries the weight of authority should include so dogmatic a statement. There are many who consider surgery a justifiable procedure for the relief of symptoms, but there is certainly more than a little doubt that it has materially lowered the rate of mortality.—I am, etc.,

Horley, Surrey. T. W. PRESTON.

Chicken-pox Repeated

SIR,—As second attacks of chicken-pox are of rare occurrence I thought that the following account of two cases in the same family would be of interest and worth reporting.

On November 12, 1951, I was called to see a boy aged 5 years, one of monovular twins. He had a pyrexia of 100° F. (37.8° C.), and had a well-developed papulo-vesicular eruption having the typical distribution of chicken-pox and which had first appeared the evening before I saw him. He had lesions in the scalp and on the soft palate, and I had no hesitation in diagnosing the condition as that of chicken-pox, as he had not long commenced to attend school and there was an epidemic of chicken-pox in the district at the time.

A few days later his twin brother developed a similar eruption with a moderate pyrexia and was obviously another case of chicken-pox.

Both boys had the normal course of the disease and were clear of the eruption and quite recovered in three weeks from the commencement of the disease in the second boy.

On December 28 I was again called to the house to see the first twin, who had broken out in another papulo-vesicular eruption that same morning. This time he had no fever, and at first I was inclined to think that he had a lichen urticatus, on account of the severity of second attacks of the chicken-pox and also because of the very recent attack which he had had.

However, the rash was again so characteristic, both in the individual lesions and in their distribution, that I was forced to accept this as another attack of chicken-pox, and when, three days later, his twin brother also broke out again in a typical eruption there was no possible doubt about it.

Both boys continued with the eruption for about ten days and were clear in a little under three weeks on this occasion.

The most remarkable feature about these two cases is the extraordinarily short interval between the two attacks, and apparently the boys became reinfected almost as soon as they returned to school after their first attack.—I am, etc.,

Birmingham. C. SPENCER WHITEHOUSE.

Proctalgia Fugax

SIR,—In notes and correspondence on the subject of proctalgia fugax (see "Any Questions?" March 22, p. 669) I have not (so far as I remember) seen it suggested that a predisposing factor for the occurrence of the painful cramps in question may in certain individuals be an unnatural condition of emptiness in the lower bowel brought about by ordinary purgatives or otherwise. I remember, though I cannot lay my hands on it, an elaborate paper published in France some years ago in which the writer stated that in certain patients by frequent *x*-ray examinations he had found that spontaneous cramp-like contractions were more likely to occur when the bowel was empty. This might help to explain occasional attacks of proctalgia fugax in relatively young persons as well as more frequent attacks in older individuals in whom other conditions such as senile constipation or abdominal atheroma are more likely to be present.—I am, etc.,

London N.W.1. F. PARKES WEBER.

Experiment in Peacemaking

SIR,—Dr. R. L. Kitching (March 8, p. 548) is asking the B.M.A. to act in a very high-minded and desirable manner. The Association consists of members who, like other members of our community, are very concerned with the prevailing social insecurity. This insecurity expresses itself as a driving concern to increase the size of one's income, which is reflected in B.M.A. thought and policy. In times past the Association was able to devote much of its time to higher things which were in keeping with the dignity of a humanitarian profession. The language used was on an equally high plane. This language is still used, but as a guise for less dignified proceedings, such as the distribution of secret awards. It is hardly likely that the state of mind in which this was done is also capable of contemplating an idea such as that which Dr. Kitching suggests, let alone the decline in social organization which makes such an idea imperative.

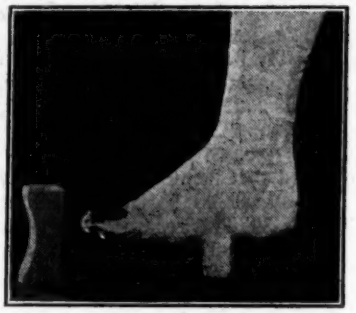
The financial and technical supremacy of the present Western civilization is rapidly drawing to a close. Within that supremacy were many fine ideas which alone can prevent our complete eclipse. Ideas are man's most precious attribute, and they will flourish wherever there is human life; bombs destroy both ideas and life. It is the duty of everyone to try to see through the present social fog and to cultivate the ideas which alone ensure survival. Military strength is, regrettably, an important factor in national policy, but by itself it is universally lethal. It must be controlled by sound ideas and ideals.

I very much doubt if the B.M.A. will be able to help in this matter.—I am, etc.,

Liverpool. H. E. VICKERS.

Wooden Heel for Walking Plasters

SIR,—I have found this wooden heel for walking plasters superior to the conventional Böhler iron and think it may be of general interest. It is fashioned from a piece of wood 3½ in. (8.8 cm.) by ½ in. (1.25 cm.) by 1½ in. (3.8 cm.) and is given a concave upper surface so that it fits closely to the underside of the plaster. It is placed in line with the anterior border of the tibia and held in place by turns of a 4-in. (10-cm.) plaster bandage.



With this heel one obviates the pivoting so common with the Böhler iron, and by being raised above the ground the base of the plaster is protected and does not tend to crack as it may when a sandal is worn. This device does not obscure a lateral *x*-ray of the tibia and fibula, and as the foot is raised only 2 in. (5 cm.) from the ground it is unnecessary to raise the heel of the other shoe. A further advantage is that it is economical.—I am, etc.,

Birmingham, 16. DONALD POTTINGER.

Ryle's Tube in Trachea

SIR,—Mr. Eric Coldrey's reference to a stomach tube in the trachea (February 16, p. 382) is interesting, but I suggest the implications are more important than is at first apparent. In Mr. Coldrey's case no ill result ensued, but it is easy to imagine a more unfavourable outcome had the tube remained undiscovered, as the following case illustrates.

Following drainage of an advanced peritonitis due to a gastric perforation, a middle-aged man was receiving intermittent suction. A radiograph to check for subphrenic abscess showed the Ryle's tube in place. Twenty-four hours later several successive aspirations were negative, but the patient soon proved the inadequacy of the suction and vomited. Afterwards he appeared no worse and was alert, complaining of no discomfort, with the nasal tube apparently still in place. During the following hour aspiration was negative and the patient became mildly dyspnoeic and cyanosed. Oxygen was given and a house-surgeon informed. On the latter's arrival he found a very apprehensive, blue, collapsed patient, complaining of intense pain in the chest and throat. Pulmonary embolism was diagnosed, but when a radiograph showed the end of the Ryle's tube in the right lower bronchus a shocked ward sister associated the patient's collapse with her attempted resuscitation before the resident's arrival: a quantity of diluted brandy had been injected into the bronchus, not, as was thought, into the stomach. The patient's failing constitution did not survive this additional setback.

In this case, no doubt general debility led to the partial suppression of the laryngeal reflexes, but this can also occur following simple catarrh, over-use of the voice, and less obvious general weaknesses such as anaemia. Patients vary in their ability to control their involuntary reflexes, and they can be exhausted by repeated or prolonged stimulation. I

have seen a resolute though uncomfortable nurse who had undergone thyroidectomy bravely tolerating an endotracheal tube several hours after recovering consciousness. The staff had instructions not to remove it until she coughed.

Galley (*Modern Practice of Anaesthesia*, 1949, p. 355) states, "It is well known that even in the conscious patient the larynx has a greater tolerance for foreign bodies which do not move." This is confirmed by Mr. Coldrey's case and an exactly similar one which occurred here recently.

It should be stressed to nurses that difficulty, coughing, straining, and retching are not normal reactions to the passage of a Ryle's tube. When these occur to excess in any patient, particularly in the exhausted, toxic, or otherwise debilitated, the tube should be under suspicion until proved, by positive gastric aspiration, to be in the stomach. Too frequently a negative aspiration is taken to mean that the stomach is empty. How often, if ever, is a stomach really dry? Tranquillity after the correct length of tubing has disappeared is in no way proof of correct position. How many emergency procedures have ended fatally from inhalation of vomitus, in spite of a Ryle's tube carefully strapped to one cheek? Not infrequently it may be too short, too fine, too soft (easily collapsed by negative pressure), or otherwise inadequate in itself. Where the distal end may be is apparently anyone's guess. Coiled in the throat is commonplace, doubled in the oesophagus frequent, and on rare occasions it may be in the trachea. I have known it carefully and purposefully concealed in the cheek—the latter the final attempt of a resourceful patient to escape from his tormenter.—I am, etc.,

Portsmouth. R. J. HAMER HODGES.

Vomiting during Anaesthesia

SIR,—In his article on "Anaesthesia for Minor Procedures" (February 23, p. 431), Dr. W. W. Mushin writes, "If the patient is known to have had a meal within three hours of the anaesthetic, it is better to postpone the operation rather than to risk the very grave dangers of regurgitation and inhalation of vomit." This statement would seem to imply that a lapse of three hours following the last meal will eliminate the danger of inhaled vomitus. In my experience, this is certainly not the case, and I fear this teaching may give the unwary a dangerous and false sense of security. To give a safe margin the interval should be much longer, for I have learnt by alarming, though happily not fatal, experiences that the stomach may not empty for as long as 12 hours after a heavy meal, especially if the patient has been the victim of trauma and shock, as in road and industrial accidents. In such circumstances, it seems to me, the stomach may empty very tardily. It may empty slowly in other conditions also, since I anaesthetized at midnight an adult male for operation for acute appendicitis, when he vomited copiously the contents of a heavy meal taken at 12.30 p.m.—i.e., 11½ hours before operation. I have had other instances of vomiting long after the accepted interval of three hours, and I feel it is a mistake to teach the occasional anaesthetist he is safe after so short an interval.

Dr. Mushin also states, "In cases of emergency, it is justifiable to empty the stomach by passing a large stomach tube just before the anaesthetic is begun." Here again I feel the inexperienced may be misled, in that, having passed his large tube and failed to aspirate any stomach contents, he may assume the stomach to be empty. Meanwhile it may be heavy-laden, and his tube blocked by a solid portion of stomach content. Such an instance demonstrates the great importance of an accurate history regarding a preceding meal. One should inquire exactly what has been partaken of—then one will know precisely what to expect.

I am myself still unhappy in anaesthetizing the unprepared emergency with, possibly, a full stomach. It is now my practice

To take a precise history of the preceding meal.

To pass a large stomach tube if this history suggests the necessity.

Not to induce with thiopentone.

Not to use relaxants unless certain the stomach is empty.

To induce by inhalation methods in order to have a quick return of the cough reflex in case of vomiting.

To induce on an operating table with shoulder rests *in situ*, to facilitate rapid assumption of a steep Trendelenburg position.

To have efficient suction apparatus ready and at hand.

To delay operation as long as possible, consistent with the interests of the patient.

—I am, etc.,

Tiverton, Devon. R. E. J. PEMBREY.

Chilblains and Hypothyroidism

SIR,—In the course of an investigation concerned with vasomotor (vegetative) endocrine disturbances and their possible influence on serum cholesterol and proteins, six female members (aged 22 to 52 years) on the staff of this hospital suffering from chilblains were examined as normal controls. Surprisingly, they all had a definite increase of cholesterol, ranging from 265 to 400 mg.%. Two were more of the athletic type, the other four more of the pycnic type. Five of them had a very delicate skin, particularly of the face. None of them showed any obvious signs of hypothyroidism, except their tendency to develop vasomotor disturbances. Their blood pressure was normal, but in three of them the pulse rate was slightly raised. Three of them had scarcely been free from chilblains during last summer and two of these had been treated unsuccessfully with vitamin K.

When the high cholesterol level was discovered, and no other reason for this fact could be seen, the increase in this substance was attributed to hypothyroidism, and a therapeutic experiment was initiated. Two persons (aged 24 and 52) were used as controls and not treated. Subsequently one of them developed chilblains and those of the other, already present, became worse with the progress of the cold season.

The other four persons (aged 22 to 48), including the two who had been treated unsuccessfully with vitamin K, were put on small doses of thyroid (¼ gr. (32 mg.) twice daily). Three or four weeks later there was scarcely any influence on the pulse rate, but their cholesterol values had come down to 240–300 mg.%, and their chilblains began to disappear, although by this time the weather had become colder and more damp.

It is interesting to note that quite a number of textbooks I consulted on endocrinology do not mention chilblains among the signs of myxoedema, although attention is always drawn to the fact that very often the first signs of hypothyroidism are hypersensitivity to low temperatures and the development of vasomotor disturbances in the skin. So possibly in outspoken myxoedema the state of the tissues, of metabolism and of vegetative-vasomotor reactivity are such as not to favour the formation of chilblains.

With regard to treatment, only few textbooks of dermatology mention thyroid as an often but apparently not always successful means of improving or curing chilblains. Gourlay (*British Medical Journal*, 1948, **1**, 336), reviewing some of the conflicting papers on the role of the thyroid and the results of thyroid treatment in chilblains, refers also to an observation of Embden (*Münch. med. Wschr.*, 1922, **69**, 201). This author, in a short note, mentions that he saw chilblains in a patient suffering from slight hypothyroidism. Treatment with thyroid proved successful. Some patients suffering from chilblains, on whom this form of therapy was subsequently applied, would benefit from it, while others would not. The author was unable to find any differences in the clinical appearances of the condition in his patients; he thought that an examination of the metabolism might help to clear the problem. A few years later, however, Barber (*Lancet*, 1926, **2**, 1180) differentiated between two main types of persons suffering from chilblains and their respective treatments: (1) the fat subjects of acrocyanosis, usually women, who react well on thyroid and iodine; and (2) the thin subjects of acrocyanosis, men and women, who react better on calcium, parathyroid, and cod-liver oil.

Thus it would appear that, among the many causes which predispose to the formation of chilblains, one is a certain form or degree of hypothyroidism (primary or secondary) found particularly in women. This may or may not be displayed together with other signs and features of sub-myxoedema. An examination of serum cholesterol with a reliable technique and at an appropriate time (blood should be taken when fasting and not about or during menstruation time; and, of course,

when other factors giving rise to an increase of cholesterol can be excluded) will usually disclose easily the presence of hypothyroidism. In such circumstances the application of thyroid hormone appears to be of value in the constitutional treatment of this condition, alone or together with other more local or symptomatic forms of therapy. It should be borne in mind that the doses I gave were very small, and also that thyroid or thyroxine treatment may not be effective during the first weeks.

—I am, etc.,

Shenley, near St. Albans. H. H. FLEISCHHACKER.

Plantar Warts in Children

SIR,—Dr. L. Forman's lucid article (March 1, p. 480) is a reminder of the heavy incidence of warts at the present time. Probably well over 50,000 cases of plantar warts in children are occurring annually. New lines of treatment or modifications of well-established procedures are being tried by dermatologists. Children can readily be approached with a stick of carbon-dioxide snow because they understand the implication of freezing. The stick can be utilized not only to produce a blister but also to provide sufficient analgesia to allow for the rapid curettage of a plantar wart.

The following technique has been employed. The child rests prone, and the carbon-dioxide snow stick, of a diameter twice the surface diameter of the wart, is applied firmly for about a minute and a half. With a sharp curette the frozen wart is immediately enucleated and the collar of hyperkeratotic skin cut away with scissors. When vasoconstriction from cold ceases there is brisk haemorrhage, and firm pressure for 15 minutes or more is necessary to stop it. The child walks home, well padded with felt. The advantage of this method is that it deals with the wart at one sitting, that no general anaesthetic is employed, and that the injection of local analgesic into the sole, which may be very painful, is avoided. The "operation" lasts only two minutes and a carbon-dioxide snow stick is quickly prepared.

The practicability of the technique was tried out in 100 successive children who presented themselves at one hospital, and who had one or at the most three plantar warts. The reactions of the children were observed and a questionary was sent to the mothers later in which they were asked about pain experienced by the children at the time of operation and afterwards. Ninety-three parents replied. Clinical results were good, two patients returned with a relapse during the investigation, one relapse was elicited from the questionary; otherwise "no trace" or a "tiny scar" was recorded. In about 50% of cases no pain at all was experienced at the time of operation, and little pain afterwards. In another 25% though there was some pain the child did not seem to mind. In the remaining 25% there was pain at the time of curettage and after, and a few children were considerably upset; 24 out of 93 mothers stated that they would have preferred a general anaesthetic for the children.

The conclusions reached were: carbon-dioxide snow freezing followed by immediate curettage provides a speedy and effective form of therapy in about three-quarters of cases of plantar warts in children. But when the wart is very large, or extremely painful and tender from previous use of caustics or through undergoing spontaneous inflammatory change, or when the child is very nervous and apprehensive, the procedure is too upsetting; in Dr. Forman's phraseology, it is "best to forbear."—I am, etc.,

London, S.W.2. MICHAEL FEIWEL.

Congestive and Simple Glaucoma

SIR,—I have read with admiration and interest Mr. S. J. H. Miller's article entitled "Symptomatology of Congestive and Simple Glaucoma" (March 1, p. 456), and would like to congratulate both him and his colleagues on their beautiful studies of ocular tension behaviour and other clinical features in chronic glaucoma both in this paper and elsewhere. These, I think, may well emerge in the future as being of far-reaching and fundamental importance. For some time, however, I have been most unhappy about this classification into congestive and simple glaucoma in the particular sense used by Mr. Miller, which appears to be taken for granted.

Corneal oedema is well known as a frequent though not constant companion of very high intra-ocular pressure. Unfortunately its appearance has become linked with the word "congestive" and appears, in orthodoxy, to compel the labelling of a case as "congestive." Study of large numbers of cases soon shows us, however, that corneal oedema without actual congestion is in fact a common occurrence. To say that corneal oedema is a warning of a congestive phase sounds rather like the statement that the passage of a Morris Eight down the street is a warning of the approach of an articulated lorry. The fact that one frequently does follow the other seems irrelevant.

For instance, were Mr. Miller's case (Fig. 1) of "simple glaucoma" to develop corneal oedema during a subsequent phase of high tension similar to that shown, is it to be relabelled "congestive"? Alternatively, if it should pass into a true congestive phase (as is possible in experience), should it be relabelled "acute simple glaucoma"? Again, if a case showing the tension curve features said to be those of congestive glaucoma (Figs. 4 and 5) shows, in a subsequent tension curve, a peak at 6 a.m. (as many of mine have done), have we to do more relabelling? The trouble, Sir, is that the closer one examines this distinction the less valid it becomes. It seems that we may safely speak of high tension chronic glaucoma (with or without corneal oedema, and sometimes passing into a congestive phase), of moderate tension, and possibly of low tension chronic glaucoma. But our detailed clinical observations do not at present support the classification into congestive and simple. Nor does our fundamental knowledge yet enable us to adjudicate on this point. Chronic congestive glaucoma is in my opinion probably a categorical misconception. The use of the appellation "simple" for one of the greatest enigmata in ophthalmology seems deplorable.

Space does not permit of a detailed discussion of presenting features (Table III), say to say that I think that periodic or constant aching of the eyes, difficulty with near work, and temporary blurring of vision are such common eye symptoms that in practice they can hardly be useful as indications of a rare disease such as glaucoma. My experience in practice and in clinical research is that the commoner presenting features are:

1. The discovery of cupping of the disk in the course of routine examination.

2. Manifestations of very high tension such as corneal oedema or even a true congestive phase.

3. Approaching blindness—that is to say, the all too common case first seen with one eye blind and the other with extensive field loss.

Only if tonometry becomes practicable on a far wider scale than at present shall we see our cases at a really early stage. This has been abundantly shown by the recent survey undertaken by the National Society for the Prevention of Blindness in the United States of America (see *Amer. J. Ophthal.*, 1948, **31**, 1324). But, of course, the future may reveal some more easily and more widely practicable diagnostic procedure.

Finally, Sir, may I plead with Mr. Miller to differentiate between "increased intra-ocular pressure" and "raised ocular tension"? "Raised intra-ocular tension" is a solecism to which, incidentally, my attention was drawn 14 years ago rather forcibly by the late Mr. Harrison Butler.—I am, etc.,

Oxford. J. P. F. LLOYD.

Cost of Treatment

SIR,—I should like to point out an apparent error in the letter of Dr. R. McL. Todd (March 8, p. 546). In the discussion of the cost of treating infections with antibiotics, he states the approximate cost of treating an infant weighing 6.8 kg. for a five-day period with "aureomycin," using the accepted dosage (25 mg./kg.), is 27s. 9d. This is not so. The figure should read 6s. 2d., which is the delivered cost of 1 g. of aureomycin to Ministry of Health hospitals which are served directly.

Recent trends clearly show that in infections in which aureomycin is indicated a dosage based on 12.5 mg./kg. body weight is effective.[1-4] The further saving in the cost of treatment is therefore considerable.—I am, etc.,

Lederle Laboratories Division, Cyanamid Products, Limited. A. T. MENNIE.

REFERENCES

1 Wright, L. T., *et al.*, *Surg. Gynec. Obstet.*, 1951, **94**, 661.
2 Flippin, H. F., *et al.*, *J. Amer. med. Ass.*, 1951, **147**, 918.
3 Douglas, R. G., *et al.*, *Med. Rec. (Houston)*, 1951, **45**, 482.
4 Basu, A. K., *Lancet*, 1951, **2**, 909.

Spontaneous Pneumothorax from Secondary Sarcoma

SIR,—The report by A. B. Shaw (*British Medical Journal*, 1951, 1, 278) of a case of spontaneous pneumothorax from secondary sarcoma of the lung, and the apparent rarity of this combination, prompt me to report a further similar case. A single secondary growth appeared six years after amputation of the right leg for synovial sarcoma, with collapse of the opposite chest wall due to an old pleural effusion and pleural fibrin bodies which showed a superficial radiological resemblance to other secondary growths.

The patient, aged 29, had his right leg amputated in 1941 for a sarcoma of the synovial membrane of the right ankle-joint. He remained well following this until four months before admission, when for 10 days he had a fever of unknown origin.

Although he then returned to work he lost weight, but had no other symptoms until eight days before his final admission, when he became rapidly more breathless until dyspnoea occurred at the slightest exertion. He had no cough. On admission he was a pale, extremely ill man, with severe orthopnea. The left chest was collapsed, but with normal air entry and no adventitious sounds. The right upper lobe was hyperresonant, with absent air entry. The right base was dull to percussion, some crepitations were present, and the air entry was diminished. There were no enlarged glands; the liver was not palpable. The urine and the blood count were normal. A radiograph showed a right pneumothorax involving the upper half of the chest. In the right lower lobe there was a shadow about the size of a cricket ball. The mediastinum was displaced to the left. The left chest was collapsed, with gross pleural thickening; two rounded shadows about the size of a penny were present, one adjacent to the diaphragm and the other in the mid-zone.

Temporary improvement followed the aspiration of 700 ml. air from the right pleural cavity. The dyspnoea returned, and 48 hours later a further 1,300 ml. was withdrawn. Aspiration three days later from the same space produced a blood-stained fluid. Several radiographs showed a rapidly increasing fluid level. Attempts at aspiration were unsuccessful, and 18 days after admission thoracotomy was performed, about two pints of clotted blood removed from the pleural cavity, and a large mass of hyperaemic friable growth found to occupy the lower part of the right lower lobe and pleura. Transpleural spread had occurred and the diaphragm was also involved. It was considered impossible to remove the growth. The patient died the following day. At necropsy there was no macroscopic evidence of secondaries elsewhere in the body. Histology of the growth showed degenerate tissue with the appearance of sarcoma, but the type could not be determined. Histology of the bodies from the left lung showed fibroblastic tissues, without evidence of malignancy.

—I am, etc.,

Plymouth. G. R. STEED.

Notification of Disease

SIR,—May I make some comments and suggestions on the subject of notification of disease, discussed in your leading article (March 1, p. 474)?

1. Statutory notification covers only infectious diseases or conditions possibly due to an infectious cause. For various reasons not all infectious diseases are notifiable.

2. The notification of the first case in the family over a prescribed period should be sufficient for measles. The health department should follow up the family for the further record, in the course of its inquiries. If whooping-cough was not likely to be the subject of an "immunization" campaign I would say the same for it.

3. Similarly, only the first case of dysentery or any acute streptococcal throat infection in a family should be notified, unless the sufferer is a food (including milk) worker, who should in every case be notified.

4. Any case of acute enteritis of uncertain cause should be notified if it occurs in a food worker or within a family in which there is a food worker.

5. Carriers of the intestinal diseases for a period exceeding a prescribed time, differing for different organisms, should be notifiable.

6. The notification of acute primary pneumonia should be abandoned. The notification of erysipelas should be abandoned. Puerperal pyrexia should be redefined—the regulations are too stringent. In any event, the practitioner should be required to state the believed cause.

7. Notification by telephone should be accepted and encouraged. Speed and accuracy are both important.

8. Medical laboratory workers should be required to notify when their findings point to infectious disease (I except venereal disease).

9. Many of us feel it was a grave mistake to divorce the isolation hospitals from the public health departments.

10. Notification of a disease is used (*a*) to ascertain its incidence (rate and location), (*b*) as a basis for control, (*c*) as a basis for further inquiry into the disease. It is the only way all the cases of a disease in the community can be ascertained, and it is necessary even to secure a random sample. It is difficult to justify statutory notification for the purpose (*c*) above, although very grave diseases susceptible to control could reasonably be held to do so.

11. The M.O.H. is the person statutorily charged with the duty of ascertaining and remedying, so far as practicable, circumstances prejudicial to the health of the inhabitants. Therefore all statutory notifications should go to him, *without exception*. If he does his duty he cannot "play the part of postman" as you suggest. He now regards all disease which may be shown to have as a substantial cause, if indirect, social or environmental factors as susceptible to some degree of control. This outlook has replaced the former, then quite essential, view that his main job was to control the infections. If general practitioners, consultants, and medical officers would work together discussing not only the notifiable but also the non-notifiable infections in the area (and family epidemics might be a fruitful field), and indeed other diseases where social and environmental factors are believed to be significant, further advances, not so spectacular as in the recent past, but very important, might indeed be possible.

—I am, etc.,

Public Health Department, Exeter. E. D. IRVINE.

Is Penicillin Dangerous?

SIR,—I read with considerable interest Mr. J. B. Oldham's letter (March 8, p. 545) on the subject of penicillin cream. It is encouraging to read from a surgeon's pen a conclusion which the dermatologists of this country arrived at some five years ago and which they have been consistently preaching ever since, both to their colleagues in general practice and also in surgery and general medicine. I have always held that the indications for the local use of penicillin in dermatology were few, and with the increasing number of resistant strains of organisms they are becoming fewer.

I had occasion recently to suggest in a letter to a senior medical officer of the Ministry of Health that the greatest single economy in dermatology would be the discontinuance of the use of local penicillin. The economy attained thereby would derive not only from saving of the cost of the penicillin, but also from the saving in time and effort on the part of practitioners spent in treating the resulting sensitization eruptions, and also of a considerable number of man-hours in industry and elsewhere.

It is to be hoped that the voice of the surgeons will carry further than that of the dermatologists.—I am, etc.,

Wolverhampton. D. E. OAKLEY.

Sulphamerazine Still Dangerous

SIR,—I feel at this time of year it may be opportune to draw attention to the frequent use of sulphamerazine in the treatment of respiratory infections, and the relatively small margin of safety afforded by this preparation against the development of urinary complications. Having just relieved a fifth case of sulphamerazine anuria, and having been called to see two instances of ureteric obstruction due to the drug within the last month, I am prompted to reiterate that extreme care is needed to ensure an adequate urinary output during treatment.

It is generally conceded that, despite its low solubility, sulphamerazine when given in the recommended dosage is reasonably safe provided that a copious water intake is maintained. Supervision of the latter, however, is sometimes difficult, particularly in the patient's home, and vomiting and surface loss, especially in children, may deplete the fluid reserves. In such circumstances the risk of urinary obstruc-

tion is ever present, and, while many doubtless relieve themselves spontaneously with the aid of additional fluid and alkalis, others less fortunate may develop complete ureteric obstruction and anuria requiring urgent instrumental relief. It seems, therefore, that the advantage gained by the more widely spaced dose of this drug should be jointly considered with the absolute necessity for maintaining close observation of the fluid intake and loss throughout treatment. Should the latter present any difficulty the choice of a more soluble sulphonamide may then be well advised.—I am, etc.,

Institute of Urology, W.C.2. J. D. FERGUSSON.

Xylocaine

SIR,—Some time ago I showed in the experimental laboratory that when given by various routes to various species of animal "xylocaine" was twice as toxic as procaine (*Brit. J. Anaesth.*, 1951, **23**, 153). On the basis of the clinical evidence then available, however, the two drugs were of approximately equal toxicity when used in the human subject. At the time no apparent satisfactory explanation of this seeming contradiction was available.

For the past few months xylocaine, 0.5% with 1:160,000 adrenaline, has been used for local analgesia in the department of neurosurgery in Manchester. This mixture has produced manifestly better vasoconstriction than the 1% procaine and 0.1% amethocaine used previously with the same amount of adrenaline. It has been known since Braun first used a vasoconstrictor in local analgesia that the effect of such drugs is to reduce the toxicity of the analgesic agent by delaying absorption. Better vasoconstriction therefore means greater reduction in toxicity. The difference in the maximum tolerated dose of xylocaine with and without adrenaline will therefore be greater than the corresponding difference when procaine is considered. It is thus possible to use amounts of xylocaine with adrenaline which by themselves would be dangerous. There are, therefore, very good grounds for Mr. C. Grimshaw's suggestion (March 1, p. 489) that the omission of the adrenaline was to some extent responsible for the fatality reported earlier in your medico-legal columns (February 2, p. 280). Also there is at last a credible explanation of the apparent contradiction that xylocaine is twice as toxic as procaine in experimental animals but about equally toxic in clinical practice.

—I am, etc.,

Manchester. A. R. HUNTER.

SIR,—We have followed the correspondence on "xylocaine" with considerable interest, as we have used it extensively for the last year. We have found that its rapidity of action, the intensity and duration of its effects, far exceed those of procaine or amethocaine and that there has been no significant toxic effects in the dosage employed (up to 1 g.) other than those attributable to the adrenaline (1:80,000) added to the 2% dental preparation. Consequently we now use it as a routine for surface application, local infiltration, and regional and epidural blocks.

For urethral instrumentation a 2% (plain) solution will rapidly produce effective analgesia, thus avoiding the 15-minute wait which is customary with other agents. By local infiltration its action develops within a few seconds and rapidly diffuses: it is effective for at least an hour with the plain solution and up to four hours with the adrenaline added.

In particular, we have found it of special value in abdominal emergencies occurring in feeble aged patients. Regional nerve block using 0.5% (plain) xylocaine solution gives rapid analgesia and muscular relaxation, and we confirm the observation that several patients have fallen asleep once the actual operation started: in each case they could be roused by the voice. The effect was reinforced, and after-pain prevented, by the use of intravenous pethidine in doses of 25 to 100 mg. The post-operative condition of these patients was incomparably better than that following orthodox general anaesthesia; shock, respiratory depression, and post-anaesthetic vomiting were absent.

In our opinion the introduction of xylocaine marks a definite advance in anaesthetic and surgical technique.—We are, etc.,

JAMES ROCHFORD.
Barnet, Herts. HENRI ROUALLE.

Whooping-cough Immunization

SIR,—Whooping-cough immunization has had such a chequered career that it was refreshing to read Professor Robert Cruickshank's views in the second part of his article on the pros and cons of immunization (February 2, p. 268). I have unwaveringly inoculated babies of 3 months old for the last six years, in the face of prejudice and opposition from some mothers and the local public health authorities, provided the baby was over 12½ lb. (5½ kg.). The weight is the main consideration after all, for one must have sufficient tissue in the upper lateral quadrant of the buttock to inject ½ ml. and also the antibody response is adequate at that weight.

Having inoculated hundreds of babies, I can say that Glaxo's "combined diphtheria pertussis vaccine" is safe and effective, and that I nowadays treat very few cases of pertussis. The latter are either suppressed pertussis in 3- and 4-year-olds who have not had a booster dose, or else children who have escaped my attentions.

I contend that post-inoculation poliomyelitis was never really proved. Some of the reported cases were wrist-drop, which may have been caused from inoculation into or near the radial nerve. If there were genuine cases they might be coincidental, and, anyway, why should not vaccination produce similar sequelae? As this piece of research was done through my local clinic I heard several different points of view.

Lastly, the local authorities should be induced to pay more than they do for the work of immunization, because it often involves a call on the mother.—I am, etc.,

Hampton Hill, Middlesex. I. E. D. MCLEAN.

Complications of Arsenotherapy

SIR,—The interesting article by Dr. M. G. Nelson (February 9, p. 300) prompts me to record a similar case of agranulocytosis and spontaneous bruising complicating arsenotherapy. In my case, however, there was no thrombocytopenia or other clotting abnormality.

The patient was a woman of 44 who, following an attack of acute bronchitis, lapsed into a state of subacute pulmonary congestion which persisted for many months. All investigations proved negative and it was difficult to account for the condition, which was resistant to all forms of antibiotic and other therapy. There was no evidence of left ventricular failure. As a last resort it was decided to give her a course of intravenous neoarsphenamine, which was successful in resolving the condition. However, following the last injection (2.4 g. total) she developed a moderately severe generalized dermatitis, which cleared up with antihistamine treatment. One month later she complained of painful and swollen knees and ankles, associated with the appearance of spontaneous bruises. The latter were numerous, measuring 1–2 in. (2.5–5 cm.) in diameter and occurring mainly on the limbs. There was no actual purpura, but the capillary-fragility test was positive. Blood investigation revealed: Hb, 13.4 g. per 100 ml. (90%); erythrocytes, 6,160,000 per c.mm., leucocytes, 3,700 per c.mm. (polymorphs 64%, lymphocytes 25%, monocytes 6%, eosinophils 5%); platelets, over 240,000 per c.mm. Clotting time (Dale and Laidlaw) 2 min. 5 sec.; bleeding time 2 min. 15 sec., prothrombin time normal compared to control.

No specific treatment was given and two weeks later the leucocyte count was down to 3,000 per c.mm. (polymorphs 50%, lymphocytes 46%, monocytes 4%). Four weeks after this the symptoms had resolved, the leucocyte count being 4,200 per c.mm. (69% polymorphs). Four months later severe spontaneous bruising recurred. It was difficult to be certain whether this was prior to or following a week's treatment with vaginal acetarsol for leucorrhoea. The white cell count was now 4,500 per c.mm., with 28% polymorphs, 68% lymphocytes, 2% monocytes, and 2% eosinophils. A course of pentose nucleotide, 10 ml. intramuscularly daily for two weeks, was then administered. On conclusion the leucocytes numbered 4,100 per c.mm. (63% polymorphs). Spontaneous bruising is considerably improved at the present date, although still occurring to a small extent.

—I am, etc.,

Twickenham. DAVID WHEATLEY.

Funnel Chest

SIR,—With reference to the operation for this condition which has been developed in America and described in your annotation (February 16, p. 370), let us pause and marshal the facts before adding another scalp to the victims of medical mythology. This is an occasion for co-operation between all branches of medicine. The paediatrician sees only young and healthy children, careless of the deformity and unaffected physically by any displacement of the heart, possessors perhaps of systolic murmurs, but fortunately not now made into invalids on that account. He can only regard operation as of unproved benefit. The surgeon sees only cases which are presented to him hungry for cosmetic cure, or, Munchausen fashion, seeking another scar on the body to match up with the scars on the mind. In America, where it is more important to have a standard physical equipment, the cosmetic appeal must be even greater. The physician in charge of the elderly sees any cases of heart failure due to this condition that may occur. May we have some evidence about this? Or are such cases merely "snow on the boots" which no one has ever seen?

A. Ochsner and M. De Bakey (*J. thorac. Surg.*, 1939, 8, 496) state that the symptoms are, "Cardiac disturbances such as dyspnoea, palpitation, precordial pain, and in rare instances decompensation; pulmonary disturbances such as dyspnoea, cyanosis, cough, and diminished vital capacity, and digestive disturbances such as dysphagia and dyspepsia. In general these patients are of asthenic habitus and usually display characteristic weakness and debility."

These sound very like the symptoms of effort syndrome, or just plain anxiety neurosis. Is operation going to cure them all, and if so would not elementary psychotherapy do the same with less risk?—I am, etc.,

Bath. H. R. E. WALLIS.

POINTS FROM LETTERS

Ryle's Tube in the Trachea

Dr. C. D. T. JAMES (London) writes: It is a fact that in an anaesthetized patient with an endotracheal tube in place a Ryle's tube passed blindly almost invariably follows the path of the tube already in place. The dangers are obvious, and it behoves any anaesthetist who is asked to pass a Ryle's tube on such a patient to do so under direct vision.

Death under Anaesthesia

Dr. J. NOEL JACKSON (Whitley Bay) writes: From time to time there are reports of deaths under anaesthesia. Some of them have the common factor of death following immediately upon the administration of stimulants intended to raise blood pressure and so forth. Sometimes these measures have been taken before sending the patient back to the ward. . . . Is it too much to suggest that where there is a theatre there should also be a recovery ward adjacent, so that skilled use of posture and the less drastic devices of resuscitation under expert supervision become the rule and not the exception?

Debauchery of Honest Words

Professor A. D. GARDNER (Oxford) writes: I cannot entirely agree with Dr. H. G. Calwell (March 8, p. 548), who feels that "spectrum of antibacterial activity" is an objectionable misuse of the word "spectrum." It seems to me a figure of speech which does not debase the meaning of the word. But the snappy title of his letter moves me to invite your condemnation of an undoubted debauchery of a precise and essential word, "epidemiology," which is being inflated by writers on social medicine and similar subjects to include the study of the frequency or incidence of diseases whether epidemic or not. The right and, as I thought, obvious meaning of epidemiology is given by the shorter *Oxford English Dictionary* as "the study of epidemics," and an epidemic is "a disease prevalent among a people or a community at a special time, and produced by some special causes not generally present in the affected locality." Therefore, to speak of the epidemiology of coronary thrombosis, or of hare-lip, or diabetes, or of any non-epidemic disease is a debasement of the currency of thought. It is of no use saying that the word is being used in its wider sense. It has no wider sense.

Obituary

G. W. M. FINDLAY, C.B.E., M.D., D.Sc., F.R.C.P.

The death of Dr. G. W. M. Findlay on March 14 was recorded in the *Journal* of March 22 (p. 658). We are indebted to Professor B. G. Maegraith for the following appreciation:

I first got to know George Marshall Findlay really well when he went to West Africa during the war. He was attached to the G.H.Q., West African Forces, as consulting physician. For the ordinary man it would have constituted a full-time job to deal with the medical problems presented by the assembly of a large European force in such an environment. Findlay was no ordinary man, and almost before they knew it the local authorities had provided part of the Medical Research Institute for work on haemolysis, malaria, viruses, and anything and everything else that turned up. This work was continued there, and in the later established laboratory in a nearby general hospital, until he left in 1945. During that period Findlay stimulated considerable research activity amongst work-hungry young Service personnel, and his kindness and enthusiasm will long be remembered by those who worked with him.

Findlay was a voracious reader. He was interested in everything. His knowledge of medical literature was encyclopaedic and his memory astonishing. Medical textbooks and journals, books, and papers on anthropology, natural history, and local history were all absorbed in turn, abstracted, and transcribed neatly in his clear, round hand into school notebooks. He once told me he had been keeping notes of this sort since he was a boy. If his notebooks have been kept they must represent a unique and wondrous store of knowledge that I hope will be preserved.

Findlay's approach to medicine was rather that of an eighteenth-century natural historian. All sides of the problem interested and excited him, and he attacked his work with a gusto and enthusiasm which sometimes seemed a little to outweigh his critical judgment. He absorbed ideas like a sponge. Every bit of information was useful and important in its proper place, no matter where it came from, and to him the natural place for it was in some permanent record. The long list of clear, well-written scientific papers which are credited to him, and particularly the remarkable new edition of his book on chemotherapy upon which he was still engaged when he died, remain as a memorial to him, but those who knew him will, I think, prefer to remember the man. Highly intelligent, amusing, intolerant of interference (especially official) or hindrance, his was the kind of inspiring, irritating, restless personality that influenced and stimulated everyone who came into contact with him. Findlay was certainly one who did not leave medicine where he found it.

KONRAD DOBRINER, M.D.

Many engaged in the biochemistry of cancer and related fields will have received with deep regret the news of the death in New York on March 10 of Dr. Konrad Dobriner of the Sloan-Kettering Institute and Memorial Hospital Centre. Born at Elberfeld on October 14, 1902, Dr. Dobriner graduated from the University of Freiburg in 1925, and shortly afterwards received the degrees of doctor of medicine and doctor of medical

science of the University of Munich. After emigrating to the United States in 1933, he worked as a research fellow in the University of Rochester Medical School from 1934 to 1936, and later for a period of three years at the hospital of the Rockefeller Institute. In 1939 he was appointed head of the department of research chemistry of the Memorial Hospital, and became a member of the Sloan-Kettering Institute in 1947, with the additional title three years later of Associate Professor of Medicine in Cornell University Medical School.

Dr. Dobriner was the author of some eighty contributions to the medical and scientific literature, either alone or jointly with such workers as C. P. Rhoads, L. F. Fieser, S. Lieberman, R. N. Jones, T. F. Gallagher, and C. C. Stock. His earlier interests lay in the field of porphyrin excretion, and later topics included the metabolism of specific carcinogens such as 1:2:5:6-dibenzanthracene, β-naphthylamine, and dimethylaminoazobenzene, and the carcinogenicity of benzidine. Of recent years he had contributed largely to the establishment of the patterns of urinary excretion of the steroid hormones in normal and pathological states, the application of infra-red spectroscopy to steroid structure and metabolism, and the study of the effects of cortisone and related steroids on the growth of experimental tumours. From these later researches he was gradually evolving a view and interpretation of the role of adrenal cortical dysfunction in the inception and development of malignant disease as a whole. A welcome visitor to England, he had taken part in various symposia at the Ciba Foundation and at other meetings elsewhere, and it was hoped that he would be present at the International Congress of Biochemistry to be held in Paris this summer. Such was not to be, and many, not only in the country of his adoption but far beyond it, will mourn "Dobie" as a valued colleague and generous friend. He is survived by his wife and two young children.—A. H.

MICHAEL HESELTINE, C.B.

The death of Mr. Michael Heseltine on March 13 was recorded in last week's *Journal* (p. 663). We are indebted to Sir Henry Cohen for the following appreciation :

The General Medical Council exerts, and is by statute entitled to exert, a greater influence on medical education and on standards of professional conduct than any other body. For the past 18 years few lives could have been more closely intertwined than those of the Council and Michael Heseltine. Others have rightly paid tribute to his superlative gifts as an administrator and to his unrivalled lucidity as a draftsman; and it is proper to acknowledge that during his term of office as Registrar, which saw fundamental changes in the constitution of the Council and its committees, it was his contribution more than any other which ensured that the transition would be smooth and the outcome workable.

But Michael was more than a great administrator. He had a genius for friendship; he was a humanist, a scholar, a wit, a historian, and a bibliophile. I recall how warmly he welcomed me as a new member of the Council, appointed during the war, shortly after the Council's offices had been bombed, and while he was carrying a well-nigh overwhelming burden of responsibility with a depleted staff; and, later, how many were the generous gifts of time and advice which were to flow from that refined and fastidious mind.

In 1946 he accompanied the President and four members of the Council on a visit to Canada and the U.S.A. to examine medical education. The smooth path we were able to follow in comfort, indeed in luxury, owed much to Michael's charm and irresistible personal magnetism. It was on this trip that was conceived the project to which he was to devote the early years of his retirement—a history of the Council and its influence on medical education.

He had great courage. He knew the nature of the illness some years ago which demanded radiotherapy. From the necrosis of the jaw which followed he suffered constant and, at times, agonizing pain; yet he persevered with all his tasks and met us all with his customary cheer and equanimity.

A personal note is not the place for an inventory of his remarkable and exceptional qualities of mind and heart. Nor, indeed, would he have wished it. He would certainly have urged that there be "No flowers, by request," for he had that essential humility which is the surest shield against intellectual arrogance.

Petronius (of whose works Michael contributed a masterly translation to Loeb's Classical Library) wrote in his *Satyricon* that "a man must have his faults" (*sed sibi quisque peccat*). Be this as it may, it can be said of Michael, without any equivocation whatsoever, that amongst members of the Council he leaves no resentments and no enmities; nothing but the memory of a gracious, witty, brave, and generous character who served them and, through the Council, our profession, with unstinted devotion and unsurpassed distinction.

Dr. H. Guy Dain writes : Everyone who has had the privilege of working with Heseltine must have fallen under the influence of his charm and kindly friendliness. To know him was to find a friend, a friend who could always be relied upon to be helpful.

His association with doctors and their problems was long and valuable. As one of the team of young Civil Servants brought together by the late Sir Robert Morant to work Mr. Lloyd George's National Health Insurance scheme, he was concerned from the beginning with the problems of the medical service. During his period of service at the Ministry of Health he took part in the discussions and developments of the "panel" service in its early days. Then, as always, he was helpful and approachable.

Deciding to leave the Civil Service, he was appointed Registrar to the General Medical Council, where his contact with doctors was not only continued but became more intimate. With the background of his experience at the Ministry of Health he interviewed both doctors and the public with sympathy and understanding. He was a master of the English written word, and his memoranda and documents were models of construction. He made himself acquainted with all the intricacies and pitfalls of the Medical Acts, so that when a new Medical Act was passed in 1950 it was Heseltine who had thought it out and worked out all the detail.

During a recent dangerous and painful illness, his friends on the General Medical Council were much impressed by the courage and fortitude that he displayed. They were delighted with the recovery he made, and when his retirement became due last year it seemed he would be able to enjoy it in reasonable health. The news of his death comes as a great shock to the Council.

Dr. EDWARD DAVISON SMITH, of Whickham, Newcastle-upon-Tyne, died on December 26, 1951, of coronary thrombosis, as his father and two brothers had done before him, and like them he died in harness. He was 67 years of age. Born into a family of doctors and brought up in an atmosphere of medicine, he naturally took to it as a vocation. He graduated M.B., B.S. at Durham University in 1908. After serving for a year as house-physician and surgeon in the Royal Victoria Infirmary, Newcastle-upon-Tyne, and going on a trip to the Far East as a ship surgeon with the Blue Funnel Line, he settled down in practice with his father in the halcyon days before the latter had changed horses for cars. In the early days he did a little surgery, and a colleague vividly remembers 40 years ago his operating for a strangulated femoral hernia on an old lady lying on a feather bed. She made an uninterrupted recovery. He served throughout the first world war in the R.A.M.C. and took part in the Gallipoli landing. He was president of the Medical Institute in Newcastle, a member of the B.M.A. and the Northern Counties Medical Society, and a regular attender at their scientific and clinical meetings. A general practitioner in the old tradition, Smith knew his patients to the third and fourth generation, and gave them not only of his clinical best, but made himself their trusted guide, philosopher, and friend. For many years he was the senior of a particularly happy partnership with his two brothers, and latterly with his nephew and another younger man. Intensely loyal to his colleagues, his enthusiasm never waned and he was at all times willing to help his juniors with a worrying case. Recently his cardiac condition worsened and increasing dyspnoea seriously limited his working capacity. He carried on to the end with a fearlessness and courage and unfailing cheerfulness of disposition which were an inspiration to all who knew him. He is survived by his wife, to whom we offer our deepest sympathy.

By the death of Dr. C. H. HALL at the ripe age of 84 the medical profession in West Hertfordshire has lost its doyen and many of its members have lost a personal friend. Charles Herbert Hall was educated at the University of Glasgow, where he graduated M.B., C.M. in 1890, proceeding M.D. in 1901. After practising for a short time in the north of England he settled in Watford in 1891, at that time a small market town in the country, very different from the large industrial centre it has since become. Dr. Hall soon developed a large and active practice and in addition held various appointments, including those of medical officer to the old St. Pancras Schools at Leavesden and to the London Orphan School, and physician to the Cottage Hospital, which later developed into the Watford Peace Memorial Hospital. On reaching the retiring age he was elected consulting physician to the latter. He formed and directed a local branch of the St. John Ambulance Brigade, and he became a governor of the Watford Grammar School for Boys and was closely associated with the Watford School of Music. His medical colleagues, however, will chiefly remember him for his successful efforts in promoting amity and friendliness among the medical practitioners of the district. He achieved this partly by quiet contacts with individuals, but mainly by the encouragement and stimulation of the long-established West Herts and Watford Medical Society, which, under his wise guidance, became a flourishing and lively centre for academic and social gatherings. He became secretary of the society on September 18, 1896, and held the office for the record period of 51 years and was able to be present at its centenary dinner in 1950. He was happily married and founded a medical family, one daughter becoming a hospital almoner and another a radiographer, while his son and grandson are both doctors practising in Watford.

Dr. HENRY CARDEN PEARSON, who died on February 18, aged 77, was educated at the University of Edinburgh, where he graduated M.B., C.M. in 1895. After holding appointments at the Royal Hospital for Sick Children, Bristol, at Birkenhead Borough Hospital, and at Staffordshire General Infirmary, he took the F.R.C.S.Ed. in 1899, and in the same year entered into partnership with the late Dr. A. H. Thompson, of Darlington, who died last August at the ripe age of 96. Dr. Pearson became house-surgeon at the old Greenbank Hospital, Darlington, in 1901, and was a surgeon at the Memorial Hospital there until 1934, when he became consulting surgeon. He was orthopaedic surgeon from 1920 until his retirement in 1939, and was the founder of the orthopaedic department at Greenbank Hospital. One of his greatest interests outside his profession was the Darlington Rotary Club, which he helped to found in 1922. He was president in 1926, and it was as chairman of the club's community service committee that he became actively engaged in work among old people, an interest which occupied a good deal of his time and enthusiasm in recent years. After helping to found the Aged People's Welfare Council he became chairman of the committee controlling nine clubs for old people, an office he held until his death. He was an active member and Past Master of the Marquess of Ripon Lodge of Freemasons, and had been an official of the Provincial Grand Lodge of Durham. When the British Medical Association met at Newcastle-upon-Tyne in 1921 he represented his constituency at the Annual Representative Meeting and was vice-president of the Section of Urology. He was also chairman of the Darlington Division from 1942 to 1945. His zest for life and his friendliness and breezy vigour will be much missed by colleagues, patients, and fellow-townspeople alike. Memorials to his professional work already exist, and others in recognition of his social welfare work are projected. He leaves a widow, two sons, one of whom, Dr. R. C. M. Pearson, is medical officer of health for Watford, and one daughter.

The sudden death of Dr. F. DE R. MARTYN on March 4 has caused much sorrow throughout the Spalding district of Lincolnshire, where he was well known. Frank de Récourt Martyn was born at Lincoln on August 18, 1877, the son of a former deputy chief constable for Lincolnshire, and was educated at Lincoln Grammar School. He received his medical training at Westminster Hospital, and qualified M.R.C.S., L.R.C.P. in 1902. Before moving to Moulton he was in practice at Sutton-in-Ashfield, Nottinghamshire. While there he became a member of the Nottinghamshire County Council and chairman of the district school managers. During the war of 1914–18 he was a captain in the R.A.M.C. and served in Mesopotamia and in India, and in the last war he was medical officer to the 2nd Holland (Spalding) Battalion of the Home Guard, holding the rank of major. A Freemason, Dr. Martyn also took a keen interest in the welfare of ex-Servicemen, and was vice-president of the Moulton branch of the British Legion. He leaves a widow, two daughters, and three sons, one of whom is Dr. Gwyn Martyn, of Sale, Cheshire.

By the sudden death on March 4 of Mr. W. MARTIN MUIRHEAD ophthalmology in the United Kingdom has lost a pivotal figure and many ophthalmologists a warm-hearted friend. Educated at Wesley College, Sheffield, and at the University of Sheffield, William Martin Muirhead graduated M.B., Ch.B. in 1911. After resident posts at Sheffield Royal Hospital his interest turned to ophthalmology, and he obtained a position which to-day would be called a registrarship. He held this post until he joined the R.A.M.C., in which he served from 1916 to 1921, for much of the time as an eye specialist. On demobilization he worked for two years in the anatomy and physiology departments at Guy's and St. Thomas's hospitals, and then held out-patient and resident posts at Moorfields, taking the D.O.M.S. of the Royal Colleges in 1927. In that year he was appointed honorary ophthalmic surgeon to Chesterfield and North Derbyshire Royal Hospital, and he held this appointment, together with that of oculist to Chesterfield education committee, until his death. In 1939 he became honorary ophthalmic surgeon to the Rotherham and Worksop hos-

pitals. His brother then joined him in practice, and they jointly provided a remarkable example of partnership in ungrudging and organized service to the area. A man of excellent clinical sense, with an unwearying capacity for work, Muirhead maintained his interest in scientific ophthalmology and cherished his links with the London of his earlier years and the chiefs he had served there. His knowledge and ability found their proper scope when he succeeded the late Dr. P. J. Hay in 1943 as secretary of the North of England Ophthalmological Society, of which he was president in 1938–9. This difficult succession and onerous responsibility he fulfilled with outstanding success, and he maintained the activity and traditional influence of the society at its old high level. To this duty he last year added the treasurership of the Midland Ophthalmological Society. Meetings of ophthalmological societies, their scientific interest and the personal associations they provided, were a delight to him, and it was unusual for him to miss any meeting in London and unthinkable if it was in the Midlands or the North of England. When the British Medical Association met at Liverpool in 1950 Muirhead served as a vice-president of the Section of Ophthalmology. To travel with him in the United Kingdom or abroad was a constant pleasure and, incidentally, a guarantee that all doors would be opened in welcome. The kindliness of his nature shone in all he did, but it was only in working with him on a society committee that his thoughtfulness and his skill in planning to draw out and encourage the diffident or neglected (or neglectful) member were realized. His modest, kindly, and widespread influence was a unifying factor among British ophthalmologists, and, while many will greatly miss him on personal grounds, many more will feel his loss to the specialty.—E. G. M.

Dr. Lawson L. Steele (Blyth, Northumberland) writes: The late Dr. ELDRED CURWEN BRAITHWAITE, whose death was recorded in the *Journal* of February 16 (p. 389), was contemporary with me at St. Bees School, Cumberland, and was noted even in those early days for his courage and cheerfulness. He took on a notorious bully, and in a fight lasting nearly half an hour so subdued the bully that life afterwards was much happier for many smaller boys. He was in the rugby fifteen, and was one of the best half-backs the school ever had. One summer on holiday in Cumberland after I had dived into 30 ft. of water from a height of 30 ft. he not only emulated my feat but persuaded his daughter to perform the dive backwards, thus implementing his frequent saying, "Everyone should be made to be tough." He admired St. Bees School and Sedburgh School for their Spartan qualities. His scholastic achievements were worthy of the sixth form to which he attained, and my Latin proses were frequently improved by his help. It is hard to believe that he has gone; one expected that such a man would have reached his century.

Medico-Legal

DEATH AFTER 19 YEARS FROM TOOTH IN LUNG

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

In March, 1932, Cyril Brown, a wheelwright aged 27, was advised by his doctor to have all his teeth extracted because they were in a very bad condition as a result of neglect, and his gums were infected. The extraction was carried out under an open ether general anaesthetic in bed at his home. All the teeth were present and were extracted at once. After the extractions had been completed the doctor who was giving the anaesthetic got the dentist to help him to raise the foot of the bed to relieve cyanosis which the patient was then experiencing.

Mr. Brown was in due course fitted by his dentist with vulcanite dentures, and continued to carry on his calling of wheelwright until in June, 1951, he began to be seriously troubled by a cough which kept him awake at night. On June 22 he had to go to bed: he was admitted to hospital, but in spite of an operation on July 18 he died on July 22.

On July 24 Dr. J. Edwards, of Sheffield Royal Hospital, performed a necropsy. He found that death was due to the bursting of cerebral abscesses into the lateral ventricles of the brain. Since there was no local cause for the pus in the brain, Dr. Edwards concluded that the infected material had probably come by the blood stream, and he investigated the lungs. At the base of the right lung, in the bronchus about 2½ in. (6.3 cm.) from the tracheal bifurcation, he found a collection of pus and in it a hard object.

This hard object turned out to be the root of a tooth, the crown of which had been destroyed by decay or possibly trauma. It was probably the first upper right premolar, and could have been dislodged by the gag during the extraction 19 years before and inhaled while under the ether anaesthetic. Although neither doctor nor dentist could recollect a tooth having been lost, the cyanosis might have been caused by inhalation of the tooth. There was no other explanation of its presence in the lung put forward at the inquest. According to the dead man's sister, it had been a family joke that one of his teeth had been lost.

Dr. Edwards said that he had never known a similar case, but had known of a part of shell casing remaining embedded in the lung for 12 years, although in that case it had entered through the chest wall. In his opinion death was due to the bursting of the abscesses, caused by bronchiectasis, which in turn was caused by the tooth. He could see no reason why the condition should have developed suddenly after the tooth had been in the lung for no less a period than 19 years.

Medical Notes in Parliament

ADJUDICATION—THE MINISTER'S STATEMENT

In a statement to the House of Commons on March 25 Mr. CROOKSHANK said: "I think the House should be informed at once of the result of the claim by general medical practitioners for increased remuneration in the National Health Service. As the House is aware, the late Government agreed to refer the doctors' claim to an adjudicator on the understanding that his award would be binding on both parties, subject to agreement being reached on an improved method of distributing doctors' incomes. The present Government continued these arrangements, and Mr. Justice Danckwerts was appointed to act as adjudicator.

"The Secretary of State for Scotland and I have now received the Adjudicator's award. Its precise effect can be determined only after more detailed study, but broadly it amounts to the award of an additional £9½m. remuneration for the year 1950–1 (the year on which the award is based) with corresponding increases for previous and subsequent years.

"While, as I say, the full calculations have yet to be made, I feel I should inform the House that—in very approximate terms—this may involve an additional charge on the Exchequer of as much as £40m. in the coming financial year to cover the period back to July 5, 1948. This means that, in spite of the serious measures of economy which have already been proposed to restrain Health Service expenditure within a ceiling of £400m., it will be necessary to seek a Supplementary Vote for this additional amount."

Dentists

In the House of Lords on March 18 the Dentists' Bill was again examined on report. Many amendments were made,

almost all of a drafting nature and moved by the Earl of Onslow, who was in charge of the Bill. In Clause 18 Lord ONSLOW moved to provide that the regulations should not permit a member of any class of auxiliary to undertake the extraction of teeth other than deciduous teeth.

The committee agreed to the amendment.

Lord Onslow later moved an amendment to provide that if any member of a class of ancillary dental workers used any title or description to suggest he possessed a status or qualification connected with dentistry other than that which he in fact possessed he should be liable on summary conviction to a fine not exceeding £50. Where the regulations did not provide for a roll or record of the class in which particulars of professional status and qualifications might be entered the subsection would still take effect.

Lord WEBB-JOHNSON asked whether Lord Onslow thought the use of the word professional was appropriate.

Lord ONSLOW thanked Lord Webb-Johnson for bringing up this point. He said the Minister would fully consider it when the Bill went through the House of Commons.

Lord ONSLOW moved to insert after Clause 25 a new clause setting out the conditions under which students might undertake dental work. He said the amendment was really a redrafted one to meet a point raised by Lord Webb-Johnson which the Government had accepted in principle on the committee stage. The House agreed to this amendment. Other consequential amendments were made and the report stage closed.

Prescription Charges

Brigadier FRANK MEDLICOTT, on March 20, asked the Minister of Health what action he was taking on the representations received from the medical profession objecting to the proposed arrangements for the collection of prescription charges by dispensing practitioners. Mr. H. F. C. CROOKSHANK replied that he was about to discuss the matter with representatives of the British Medical Association.

Mr. GEOFFREY DE FREITAS asked what representations had been received from local medical committees in Lincolnshire that dispensing rural practitioners should not be made responsible for the collection of 1s. for medicines dispensed.

Miss PAT HORNSBY-SMITH replied that one of these committees had represented that dispensing doctors should not be responsible for the collection of the charge. Representations made by the Trades Union Congress against the proposed Health Service charges were discussed by Mr. Crookshank on March 19 at a meeting with representatives from the T.U.C.

The National Health Service Bill was discussed on second reading in the House of Commons on March 27 after we went to press.

The Services

The *London Gazette* has announced the following appointments in recognition of non-operational services in Japan in connexion with operations in Korea:

O.B.E. (Military Division).—Major (Temporary Colonel) C. W. Nye, E.D., R.A.A.M.C.

M.B.E. (Military Division).—Lieutenant (Temporary Major) J. W. F. Lloyd, R.A.A.M.C.

Major-General F. Harris, C.B., C.B.E., M.C., late R.A.M.C., has been appointed Director-General, Army Medical Services, with the rank of Lieutenant-General from April 1, in succession to Lieutenant-General Sir Neil Cantlie, K.B.E., C.B., M.C., late R.A.M.C.

Colonel J. E. Rusby, M.C., T.D., J.P., R.A.M.C., T.A., has been appointed Honorary Colonel of a T.A. Unit, in succession to Lieutenant-Colonel (Honorary Colonel) A. C. Haddow, T.D., R.A.M.C., T.A., whose tenure has expired and who retains the rank of Honorary Colonel.

Flying Officer G. A. Faux, M.R.C.S., L.R.C.P., R.A.F., Medical Officer, Royal Air Force Station, Horsam St. Faith, has received the Queen's commendation for brave conduct for helping to remove the crew from a crashed aircraft.

Universities and Colleges

UNIVERSITY OF OXFORD

The Board of the Faculty of Medicine has co-opted Dr. A. H. T. Robb-Smith for the statutory period of two years from the first day of Trinity Term, 1952.

H. R. Ing, D.Phil., has been reappointed Reader in Chemical Pharmacology from October 1, 1952, to September 30, 1959, and the following have been reappointed University Demonstrators in the subjects indicated in parentheses: Dr. R. Barer (Human Anatomy—part-time); Dr. J. M. Walker (Pharmacology); Dr. D. S. Parsons and Dr. R. H. Nimmo-Smith (Biochemistry).

Dr. C. W. Wheeler-Bennett has been appointed representative of the University on the governing body of Steyning Grammar School.

Sir Howard Florey, F.R.S., Professor of Pathology in the University, has been reappointed a member of the University and Employees Joint Committee for four years from the first day of Hilary Term, 1952.

In a Congregation held on March 1, the following degrees were conferred:

D.M.—W. H. H. Andrews, R. I. K. Elliott, H. A. W. Forbes, *A. Batty Shaw, *E. A. Spriggs.

B.M.—*Mrs. Pauline O'Neill.

*In absence.

UNIVERSITY OF CAMBRIDGE

Denis Haigh Marrian, Ph.D., has been appointed an Assistant Director of Research in Radiotherapeutics, from January 1 for five years. (*Corrected announcement.*)

Dr. Vincent Brian Wigglesworth, F.R.S., Reader in Entomology, has been appointed Quick Professor of Biology in the University for the period October 1, 1952, to September 30, 1955, in succession to Professor David Keilin, F.R.S.

Dr. K. C. Dixon has been reappointed University Lecturer in Chemical Pathology from October 1, 1952, and Dr. M. M. Bull University Lecturer in Anatomy from April 1, 1952, both to the retiring age. Dr. C. C. D. Shute has been appointed University Demonstrator in Anatomy from April 1, 1952, for three years.

In Congregation on March 8 the following degrees were conferred:

M.D.—*J. G. Selwyn, *J. P. Henry, S. C. Gold, A. S. Mason, C. F. Barwell.

M.B., B.CHIR.—*T. H. Morgan, J. H. F. Batstone.

*By proxy.

UNIVERSITY OF LONDON

The following candidates have been approved at the examinations indicated:

ACADEMIC POSTGRADUATE CERTIFICATE IN TROPICAL MEDICINE AND HYGIENE.—*London School of Hygiene and Tropical Medicine:* P. A. Cooper, E. B. Harvey, J. Newsome.

ACADEMIC POSTGRADUATE DIPLOMA IN MEDICAL RADIOLOGY (DIAGNOSIS).—*Part 1:* D. A. B. Ashcroft, A. Berezowski, M. E. Berk, A. S. Bligh, D. Brink, N. L. Bucky, H. Fateh, B. C. Hale, M. A. Harris, K. N. Kamdar, J. K. Lundie, G. A. Medhurst, J. L. Morris, D. MacK. K. Muir, I. A. H. Munro, E. Price, L. J. Sandell, J. V. Tillett, L. E. Wolpert, M. Ziman, I. Yentis.

Dr. W. D. M. Paton has been appointed to the University Readership in Pharmacology and Therapeutics tenable at University College and University College Hospital Medical School.

UNIVERSITY OF BIRMINGHAM

At the annual meeting of the Court of Governors held on February 21 Dr. H. Thwaite was appointed a Life Member of the Court, and the title of Emeritus Professor was conferred upon Dame Hilda Lloyd, formerly professor of obstetrics and gynaecology in the University.

Professor T. L. Hardy has been invited by the Council to continue to hold his University appointment as part-time Professor of Gastroenterology for a period not exceeding three years after he has ceased to hold his hospital appointment next month.

Dr. David Mendel has been appointed National Coal Board Research Fellow in the Department of Medicine from January 1.

The University is founding an additional special lectureship in the Faculty of Medicine to be known as "The Leonard Parsons Memorial Lectureship."

A bronze head of Dame Hilda Lloyd has been completed by Mr. Jacob Epstein, R.A., and a presentation ceremony is being arranged.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending March 8 (No. 10) and corresponding week 1951.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire	1951 Eng. & Wales	1951 Lond.	1951 Scot.	1951 N. Ire.	1951 Eire
Diphtheria	38	4	14	1		46	3	18	0	2
Dysentery	639	62	71	4	4	1,449	181	297	16	3
Encephalitis, acute	6	1	0	0		3	1	0	0	
Enteric fever:										
Typhoid	0	0	1	0		11	2	2	0	0
Paratyphoid	6	0	2(B)	0		4	0	1(B)	0	
Food-poisoning	94	14		2		89	8		0	
Infective enteritis or diarrhoea under 2 years				11	22				24	28
Measles*	6,883	218	561	239	222	29,067	3501	359	93	89
Meningococcal infection	57	7	25	0	6	44	4	19	1	2
Ophthalmia neonatorum	46	5	17	0		48	3	20	0	1
Pneumonia†	1,143	60	579	16	5	1,027	51	246	14	16
Poliomyelitis, acute:										
Paralytic	13	0	2	4		9	0	1	1	1
Non-paralytic	6	0				4	0			
Puerperal fever§	232	37	10	0	3	86	9	15	1	
Scarlet fever	1,581	149	221	29	80	1,056	53	165	36	61
Tuberculosis:										
Respiratory			148	42				180	31	
Non-respiratory			44	15				22	6	
Whooping-cough	2,918	114	341	112	45	5,637	420	806	56	105

DEATHS in Great Towns	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire	1951 Eng. & Wales	1951 Lond.	1951 Scot.	1951 N. Ire.	1951 Eire
Diphtheria	0	0		0	0	*0*	0	*1*	0	0
Dysentery	0	0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0		0		*0*	0	*0*	0	
Infective enteritis or diarrhoea under 2 years	11		1	1	0	*14*		*2*	2	1
Influenza	45	5	29	0	0	*130*	13	*3*	3	4
Measles		0	1	0	1		1	*1*	0	0
Meningococcal infection		3	1				1	*0*		
Pneumonia	349	55		8	10	*297*	46		9	12
Poliomyelitis, acute	2	0			0	*2*	0			0
Scarlet fever		0		0	0		0	*0*	0	0
Tuberculosis:										
Respiratory	160	19	17	3	12	*184*	18	*18*	4	11
Non-respiratory		1	4	2	4		7	*6*	2	2
Whooping-cough	3	0		2	1	*9*	1	*1*	0	0
Deaths 0–1 year	275	28	37	10	19	*303*	31	*34*	11	21
Deaths (excluding stillbirths)	6,399	907	776	140	217	*6,310*	1030	*714*	146	245
LIVE BIRTHS	7,954	1208	884	223	427	*7,453*	1268	*911*	207	417
STILLBIRTHS	204	17	30			*206*	23	*33*		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Influenza in Glasgow

We are indebted to Dr. Stuart Laidlaw, medical officer of health for Glasgow, for the following report: Influenza due to virus A was present in Glasgow in January, 1951. During the course of the present winter another outbreak of influenza occurred in the community. The prevalence of the present outbreak is best shown by the increase in the figures of the Ministry of National Insurance "first certificates," which rose from 2,991 for the week ending January 1, 1952, to a maximum of 9,772 for the week ending March 4. Even allowing for a seasonal rise to some 4,000, it is known that more than 50% of the excess over the normal figures has been accounted for by influenza. A similar trend is shown in the notifications of primary pneumonia, which rose from 99 in the first week of January to 300 in the week ending March 8, and in influenzal pneumonia, which was practically absent in January but increased to 36 in the third week of February. School attendances were also affected by the outbreak and showed the progression of the illness through the city, beginning in the south side and spreading to the north, the difference in time of incidence being approximately three weeks. In some schools absenteeism approached the 25% level, and 15–20% was very frequently recorded. No true record can be obtained of the number of individuals who have been infected, but from the information available to the Department it has been estimated that between 70,000 and 100,000 persons in the city have been affected. This gives a morbidity rate of roughly 10%. All age groups have been involved, although children over the age of 5 years and adults predominate.

Symptomatology.—The illness was of three to four days' duration, the symptoms being running nose and eyes, feverishness, headache, sore throat, laryngitis, pains in the limbs, and frequently epistaxis. Temperatures at the onset of the illness were between 100° F. (37.8° C.) and 103° F. (39.4° C.), and the pulse rate was correspondingly increased. The large majority of cases resolved without complication, but influenzal pneumonia has to some extent complicated the picture. Relapses have occurred in a number of cases about a week to 10 days after the initial illness, and have taken the form of a bronchitic cough and occasional gastric upset. The cases admitted to hospital responded well to treatment, and deaths in hospital were few.

Severity.—The epidemic, although widespread, had a low mortality rate. Deaths from respiratory diseases have risen from 21 to 94 per week compared with 155 deaths during the second week of January, 1951, when the virus-A outbreak was at its peak. The death rate for the city has not risen above 20 per 1,000 in any week as contrasted with the maximum of 28.6 per 1,000 during the worst week of the 1951 outbreak.

Virology.—Serological tests on specimens from a variety of sources examined at the Brownlee Virus Laboratory, Ruchill Hospital, Glasgow, have indicated that the causative virus is of the influenza-B strain. The causative virus itself has been isolated at the Colindale Laboratory, London. Several patients who were admitted to hospital during the second week of February suffering from influenzal pneumonia showed titres indicative of infection some 10 days previously, and from these tests it is obvious that the virus was present in the community during the first week of February. Although the outbreak is not yet over, the indications are that the disease is definitely on the wane.

Smallpox in Lancashire

During the week ending March 22, 16 cases of variola minor were notified. All are associated with the focus in Rochdale C.B. There have been no deaths, and there is no report of the disease elsewhere. Up till March 22, 110 cases had been notified.

Infectious Diseases

Infectious diseases were more prevalent in England and Wales during the week ending March 8, and increases in the number of notifications were recorded for measles 650, whooping-cough 129, scarlet fever 75, and acute pneumonia 82.

The rise in the incidence of measles was mainly contributed by three counties—Lancashire 201, Cheshire 139, and Yorkshire West Riding 132. The largest fall in the number of notifications of measles was 61 in Middlesex. The rise in the incidence of whooping-cough was mainly contributed by Wales, where the number of notifications increased by 89 (Anglesey 27 and Monmouthshire 26). The local trends of scarlet fever showed only small variations from the preceding week. The number of notifications of diphtheria were 5 more than in the previous week, but no change of any size occurred in the local returns.

For the first time in recent years no case of typhoid fever was notified in the country.

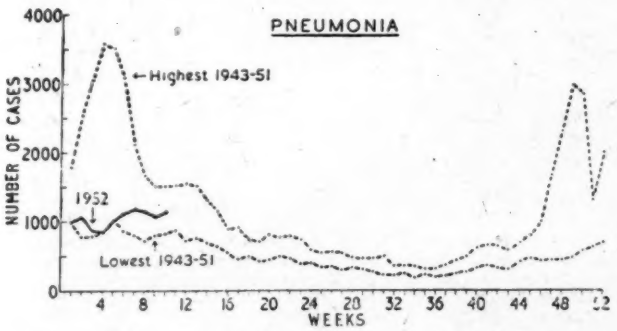
Notifications of acute poliomyelitis were 2 fewer for paralytic cases and 2 more for non-paralytic than in the preceding week. The only counties with more than one case were Warwickshire 4 (Birmingham C.B. 3) and Yorkshire West Riding 4.

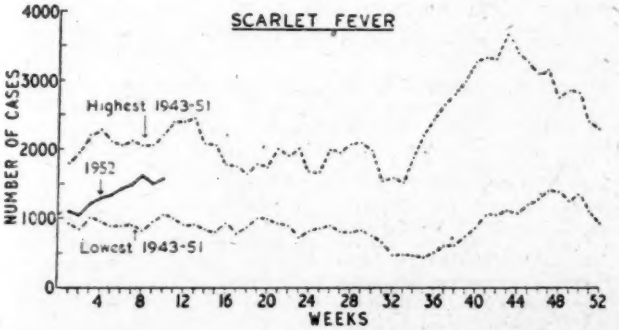
In Lancashire 62 cases of smallpox were notified; these were reported from Rochdale C.B. 59, Heywood M.B. 1, Littleborough U.D. 1, Milnrow U.D. 1.

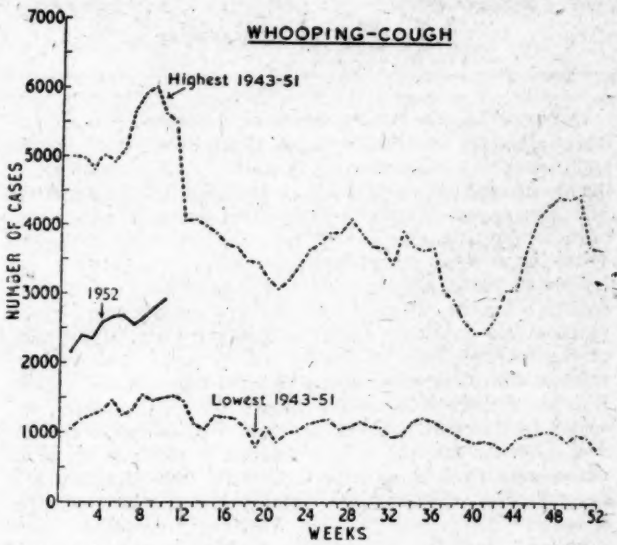
The notifications of dysentery were 8 fewer than in the preceding week. The largest returns were Lancashire 135 (Oldham C.B. 46); London 62 (scattered over 16 boroughs); Norfolk 63 (Norwich C.B. 49); Middlesex 45 (Enfield U.D. 14, Hayes and Harlington U.D. 10); Southampton County 43 (New Forest R.D. 30); Yorkshire West Riding 33 (Bradford C.B. 12); Dorset 27 (Dorchester M.B. 25); Surrey 21 (Esher U.D. 12); Warwickshire 21 (Coventry C.B. 11).

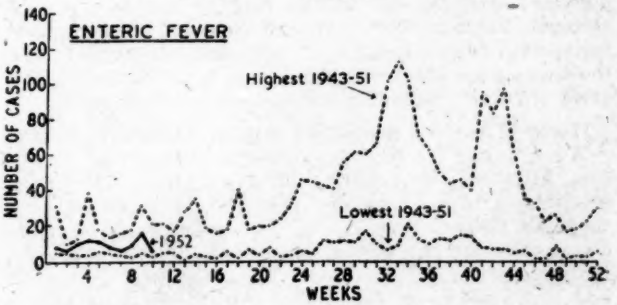
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1943–51 are shown thus - - - - - - - -, the figures for 1952 thus ————. Except for the curves showing notifications in 1952, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Road Accidents in January

Accidents on the roads of Great Britain in January resulted in 14,195 casualties, including 377 killed and 3,347 seriously injured. Compared with January, 1951, there was an increase of 678 in the total and of 13 in the killed. The chief increases were in the figures for pedal cyclists, which rose by 199 to 2,709, and those for passengers in vehicles, which rose by 255 to 3,543. Despite the continued upward trend, the accident figures for January were still considerably below those for January, 1938, when 15,745 casualties, including 514 killed, were reported.

Week Ending March 15

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,546, whooping-cough 3,086, diphtheria 53, measles 7,121, acute pneumonia 950, acute poliomyelitis 22, dysentery 642, paratyphoid fever 7, and typhoid fever 4.

That trachoma is curable and should be considered a disease which in general is only mildly contagious, except to young children, are the main conclusions of the W.H.O. Expert Committee on Trachoma which met in Geneva for its first session March 3 to 8, under the chairmanship of Professor Giambattista Bietti, of Parma, Italy. A treatment combining sulphonamides and certain antibiotics is said to be completely effective against most cases of trachoma. "Aureomycin" and terramycin are considered to be the drugs of choice. Trachoma control measures should include all the allied eye infections as well as epidemic conjunctivitis, the committee said, and it recommended a model control programme for this entire group of diseases which can be applied in underdeveloped countries. The plan calls for special legislation for health education of the people, and for a special organization, including fixed and mobile clinics attached to a trachoma institute. The important part that can be played by school-teachers in case-finding and treatment was emphasized.

Medical News

Devon and Exeter Medico-chirurgical Society.—At a meeting on January 24 Mr. Raymond Hinde spoke on "Tonsils and Adenoids: Dogmas and Doubts." The physiology of the tonsils and adenoids, he said, is imperfectly understood. The pharyngeal lymphoid tissue is functional only from birth to puberty, after which time the adenoids disappear. There is a close morphological relationship between the lymphoid tissue of Waldeyer's ring and that of Peyer's patches; indeed, when the tonsils are swollen the Peyer's patches also enlarge. Tonsillar changes occur at the time of the first dentition at the age of 2½ years, and enlargement at that time may be due to local sepsis in the mouth. But far oftener it is in the nature of a hyperplasia, the sequel of a physiological rather than a pathological change, and it is not possible to tell whether a tonsil is septic or not merely by looking at it. A swab from the tonsils is never sterile. Only when a crypt becomes sealed off does it become a source of sepsis. However, the tonsils are a portal of entry for the tubercle bacillus, and some 4% of all tonsils removed show giant-cell systems. In diagnosis it is important to remember that mouth-breathing may be due to factors other than nasal obstruction by adenoids, and not every child who keeps his mouth open breathes through it.

North of England Obstetrical and Gynaecological Society.—A meeting of the society was held in the Medical Institution, Liverpool, on February 22, when Dr. F. Da Cunha described a case of massive haemorrhage following anticoagulant therapy in pregnancy, Dr. Joseph Firth described a case of severe post-partum haemorrhage finally treated by hysterectomy, and Mr. S. B. Herd reported a case of apparent sarcoma of the ovary. Mr. L. W. Cox gave a short paper on intestinal diverticulitis and the gynaecologist, and Dr. S. J. Barr read a short paper on pressure effects of fibroids in pregnancy.

Brazilian Congress of Proctology.—The first Brazilian proctological congress was held from November 14 to 17, 1951, in Rio de Janeiro, a great many specialists from several American countries taking part. The congress was promoted and organized by Dr. Walter Gentile de Mello, president of the Brazilian Proctological Society. The *Annals* of the congress will be published in two volumes, already in preparation, with a summary of each lecture and paper in English. The editors are Drs. W. Gentile de Mello and Manoel Garcia, Avenida Graça Aranha, 81, Rio de Janeiro, Brazil.

Emergency Bed Service: Applications and Admissions.—During the seven days ending March 24 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 1,100, of whom 89.75% were admitted.

COMING EVENTS

Wessex Rahere Club Dinner.—The spring dinner will take place at the Royal Clarence Hotel, Exeter, on Saturday, April 19. Mr. C. Naunton Morgan will be the guest of honour. Further details will be circulated to members and any other Bart's men practising in the West Country who will get in touch with the hon. secretary, Mr. A. Daunt Bateman, 3, The Circus, Bath.

Osler Club.—The next meeting of the club will take place on Friday, April 18, at the Wellcome Research Institution, Euston Road, London, N.W.1 at 7.45 p.m. The evening will be devoted to Leonardo da Vinci (whose quincentenary falls on April 15), and the opening paper, by Dr. K. D. Keele, will be on "Leonardo the Physiologist."

Medical Art Society.—The annual exhibition of members' work will be held at Walker's Galleries, New Bond Street, W.1, from April 21 to May 3. Receiving day Monday, April 7. The annual dinner will be held on April 21.

Health and Tuberculosis Conference.—The conference will be held in London from July 8 to 13 and is open to all interested in preventive medicine. Subjects for discussion include protective vaccination, contemporary ideas in the management of the tuberculous patient, the social worker and the tuberculous family, the patient in industry, and tuberculosis in British Colonial territories. All information can be obtained from N.A.P.T., Tavistock House North, Tavistock Square, London, W.C.1.

Courses on Mental Defectives.—The Extra-mural Department of the University of London, in co-operation with the National Association for Mental Health, is organizing a course for medical officers on educationally subnormal children and mental defectives which will be held May 5 to 23 and repeated October 6 to 24 at the University Examination Hall, South Kensington. Full details and application forms may be obtained from the National Association for Mental Health, 39, Queen Anne Street, W.1. The total cost is £15.

International College of Surgeons.—The following meetings are announced: The French Chapter, University of Bordeaux, May 13 and 14. The Spanish Chapter (Catalonian Section), University of Barcelona, May 16, 17, and 18. International Assembly, University of Madrid, May 20 to 23. The Austrian Chapter, Vienna, May 26 and 27. The Dutch Chapter, Amsterdam, May 29 and 30. Fellows desirous of information or wishing to attend any of these meetings should make early application to the secretary of the British Chapter, Dr. J. F. Brailsford, 20, Highfield Road, Edgbaston, Birmingham, 15.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday, April 1

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—5 p.m., *"Structural and Functional Adaptation in Renal Failure,"* Lumleian Lecture by Professor Robert Platt. (See also April 3.)

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5 p.m., *"Cataract Extraction,"* by Mr. T. M. Tyrrell.

Wednesday, April 2

BIRMINGHAM MEDICAL INSTITUTE: MIDLAND MEDICAL SOCIETY.—At Queen Elizabeth Hospital, Birmingham, clinical meeting.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—5 p.m., *"Peripheral Aneurysm and Arteriovenous Fistula,"* Hunterian Lecture by Professor S. M. Cohen.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5.30 p.m., *"Visual Fields,"* by Mr. Howard Reed.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, London, W.—3.30 p.m., *"Disturbances of Sleep in Children,"* by Professor R. S. Illingworth.

YORKSHIRE SOCIETY OF ANAESTHETISTS.—At Leeds General Infirmary, 8 p.m., *"Theoretical and Practical Aspects of Therapeutic Nerve Blocking,"* by Dr. G. Steel.

Thursday, April 3

BIRMINGHAM MEDICAL INSTITUTE: SECTION OF ODONTOLOGY.—At 154, Great Charles Street, Birmingham, joint meeting with British Dental Association, Central Counties Branch. *"Oral Cancer, with Special Reference to Radiotherapy,"* by Mr. W. H. Bond. Annual general meeting will follow.

FACULTY OF HOMOEOPATHY.—At Royal London Homoeopathic Hospital, Great Ormond Street, London, W.C., 5 p.m., *"Homoeopathy and the Hypothalamus,"* address by Dr. T. F. Stewart.

OXFORD UNIVERSITY.—At Radcliffe University, Oxford, 5 p.m., *"The Significance and Mechanism of Menstruation,"* Litchfield Lecture by Dr. T. N. MacGregor.

ROYAL ARMY MEDICAL COLLEGE.—At Lecture Theatre, John Islip Street, London, S.W., 5 p.m., *"The Treatment of Hypertension,"* by Professor M. Leonard Rosenheim.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—5 p.m., *"Structural and Functional Adaptation in Renal Failure,"* Lumleian Lecture by Professor Robert Platt. (See also April 1.)

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—5.30 p.m., *"Intracranial Thrombophlebitis,"* Otolaryngology Lecture by Sir Charles Symonds.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5.30 p.m., *"Detachment of the Retina,"* by Miss M. Savory.

Friday, April 4

EUGENICS SOCIETY.—At 26, Portland Place, London, W., 5 p.m., *"The Genetics of Mental Deficiency,"* Galton Lecture by Dr. J. A. Fraser Roberts.

●INSTITUTE OF DISEASES OF THE CHEST AND INSTITUTE OF CARDIOLOGY.—At London School of Hygiene and Tropical Medicine, Keppel Street, W.C., 5.30 p.m., *"Cardiac Trauma,"* by Mr. Norman Barrett.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—5 p.m., *"After Fifty-six Years,"* Lister Oration by Sir James Learmonth.

SOCIETY OF ANAESTHETISTS OF SOUTH WALES.—At Cardiff Royal Infirmary, 7.30 p.m., films on anaesthetics.

WHIPPS CROSS HOSPITAL MEDICAL SCHOOL SOCIETY, Whipps Cross Hospital, London, E.—8.30 p.m., *"Diarrhoeas of Bacterial Origin,"* by Dr. Joan Taylor.

APPOINTMENTS

CONNOLLY, EUGENE V., M.B., B.Ch., D.P.H., D.C.H., County Medical Officer of Health, Longford, Eire.

DEWAR, R. DUNCAN, M.B., Ch.B., D.P.H., Medical Officer of Health for the Metropolitan Boroughs of Bethnal Green and Poplar.

GRAY, H., M.D., D.P.H., Assistant County Medical Officer and Medical Officer of Health, Bulmer Combined Area, Yorkshire.

HAGGER A. O., M.R.C.S., L.R.C.P., Assistant Medical Officer, Eastern Region, British Railways.

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—*Part-time Consultant Anaesthetist, Queen Elizabeth Hospital for Children.* Mrs. Dorothea B. I. Halstead, M.B., Ch.B., D.A., D.C.H. *Full-time Consultant Pathologist, Group Laboratory, Mile End Hospital,* W. D. Linsell, M.D. *Part-time Consultant Physician, St. Andrew's Hospital, Billericay,* I. Gilbert, M.D., M.R.C.P. *Part-time Consultant Physician, St. George-in-the-East Hospital,* A. S. Mason, M.B., B.Ch., M.R.C.P. *Part-time Consultant E.N.T. Surgeon, East Ham Memorial and Runwell Mental Hospitals,* N. A. Punt, F.R.C.S.Ed., D.L.O. *Part-time Consultant Surgeon, St. Andrew's Hospital, Bow,* G. A. Barclay, M.B., B. Chir., F.R.C.S. *Full-time Consultant Surgeon, Colchester Group of Hospitals,* R. N. Jones, M.Chir., F.R.C.S. *Maximum Part-time Consultant Surgeon, North Middlesex Hospital and Annexes,* K. A. Moore, M.B., B.S., F.R.C.S. *Part-time Consultant Surgeon, Prince of Wales's and St. Ann's Hospitals,* E. E. O'Malley, M.Ch., F.R.C.S.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Clayton.—On March 17, 1952, at the Garrett Anderson Maternity Home, London N.W., to Barbara E. Clayton, Ph.D., M.B., Ch.B., wife of William Klyne, a son.

Manson.—On February 25, 1952, at Salisbury, Southern Rhodesia, to Joce, wife of Dr. John M. S. Manson, of Kanye, Bechuanaland Protectorate, a daughter.

Morel.—On March 22, 1952, at Barnstaple, Devon, to the wife of Mervyn Morel, M.B., F.R.C.S., a daughter.

Muir.—On February 25, 1952, in London, to the wife of Ian Muir, M.B.E., F.R.C.S., a son.

Naidoo.—On February 18, 1952, in London, to Sandhya Bose, M.A., wife of Dr. D. Naidoo, a son—Satyadatta.

Powell-Tuck.—On March 20, 1952, at Netherwood, Solihull, to Catherine, wife of Dr. G. A. Powell-Tuck, 7, Milverton Road, Knowle, Warwicks, a brother for Jeremy.

MARRIAGES

Jenkins—Evans.—On March 16, 1952, at Gilfach Goch, Glam., Ritchie T. Jenkins, M.B., B.Ch., M.R.C.P., to Eileen Joyce Evans, M.B., B.Ch.

DEATHS

Berkeley.—On March 17, 1952, Augustus Frederic Millard Berkeley, L.R.C.P.&S.Ed., L.R.F.P.S., of 183, Kennington Road, London, S.E., aged 83.

Black.—On March 15, 1952, at 4, Anglesey Road, Alverstoke, Hants, Francis George Hamilton Rolle Black, M.B., Ch.B., Surgeon Captain, R.N., retired, aged 69.

Bramwell.—On March 21, 1952, at 29, Ormidale Terrace, Edinburgh, Edwin Bramwell, M.D., Hon. LL.D., F.R.C.P., F.R.C.P.Ed., aged 79.

Consul.—On December 26, 1951, Bishambar Dayal Consul, L.M.S.S.A., of "Vidya," Colchester Road, Harold Park, Romford, Essex.

Costello.—On March 17, 1952 at "Clare," Hulham Road, Exmouth, Devon, James Joseph Costello, L.R.C.P.&S.I. & L.M.

Coullie.—On March 17, 1952, at Dimbiecroft, Alton, Staffs, Alexander Glover Coullie, M.D., F.R.C.S.Ed., Lieutenant-Colonel, I.M.S., retired.

Crosfield.—On March 20, 1952, at Old Tolmers, Broadstairs, Kent, Arthur Mellor Crosfield, L.R.C.P.&S.Ed., L.R.F.P.S., formerly of Belgrave, Leicester, aged 79.

***Ellis.**—On March 18, 1952, at Gorleston Hospital, Edward Alfred Ellis, M.B., B.Ch., of 147 Lawn Avenue, Great Yarmouth, aged 49.

Ellison.—On March 19, 1952, at the Royal Northern Hospital, Philip Oswald Ellison M.B., B.S., of Buckhurst, Gerrards Cross, Bucks.

Ferguson.—On March 20, 1952, at his home, 29, Coudray Road, Southport, Lancs, James Ferguson, L.R.C.P.&S.Ed., L.R.F.P.S.

McElligott.—On March 19, 1952, Maurice Gerald McElligott, F.R.C.S.I., D.P.H., of Mount Rivers, Listowel, Co. Kerry, late of Bushey Heath, Herts, aged 83.

Reid.—On March 14 1952, Henry Charles Cecil Reid, M.B., B.Ch., of "Elstow," Hartley Park Villas, Plymouth.

Tacey.—On March 22, 1952, at Woodford, London, E., Dalton William Tacey, M.R.C.S., L.R.C.P., aged 76.

Talbot.—On March 20, 1952, at Prospect House, Mottram, near Manchester, Ernest Talbot, M.C. M.B., Ch.B.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Aetiology of Coronary Disease

Q.—*What aetiological relationship, if any, has mild but prolonged hyperpiesia to coronary artery disease?*

A.—The exact aetiology of coronary artery disease, meaning obliterative coronary sclerosis, is unknown. A number of factors, some of which are perhaps no more than contributory, are well recognized. For instance, there are hereditary aspects, coronary disease at certain ages being twice as common amongst the parents of those stricken with a coronary thrombosis than amongst controls. Similarly, coronary disease is common in those of "stocky build." There is evidence to suggest that a certain psychological background—the successful "go-better" type—prepares the way for coronary mischief. It is also claimed, probably with more justification, that arteriosclerosis is a biochemical disorder involving cholesterol, phopholipids, and uric acid. Hypertension may have a similar background. At all events hypertension is found in approximately 50% of men and 75% of women handicapped by angina pectoris, which is the commonest manifestation of coronary disease. On the other hand, hypertension is unusual amongst males stricken with myocardial infarction before the age of 40 years. It therefore appears that hyperpiesia is not an essential factor in the production of coronary sclerosis. It is, however, a very common associate. Even mild but long-continued hypertension must impose a strain on the arteries and aggravate, if it does not indeed predispose to, intimal vascular damage. It is usually true that to the individual the sclerosis, which is not necessarily an irreversible process, is more harmful than the hypertension.

Diet in Toxaemia of Pregnancy

Q.—*What dietetic treatment is advised nowadays in toxaemia of pregnancy?*

A.—Of recent years the importance of diet restriction has been emphasized not only in the treatment but also in the prevention of pregnancy toxaemia. By controlling the weight of a woman during pregnancy the incidence of toxaemia can be reduced. It is the sudden and rapid increase of weight that is the danger sign. Some obstetricians view an increase of more than ½ lb. (227 g.) a week as abnormal and try to limit the total gain throughout pregnancy to 20 lb. (9.08 kg.). The abnormal weight gain in many pregnant women is due to perversion of appetite and the excessive ingestion of food of high caloric value (carbohydrate and fat). When there has been a too rapid increase in weight the mother should be carefully questioned about her diet. She should be told not to use salt in cooking or at table, not to take bicarbonate of soda as a medicine, and not to take any "salts."

The following diet* can be taken as an out-patient, and has a caloric value of 1,800: 1½ pints of skimmed milk daily. *Breakfast:* tea or coffee with milk, no sugar; 2½ oz. salt-free bread; ½ oz. salt-free margarine; 1 egg; 4 oz. orange or fruit juice. *Mid-morning:* tea or coffee with milk, no sugar. *Lunch:* 3 oz. lean beef, 6 oz. potato, 6 oz. green vegetable, ½ oz. rice with milk, 4 oz. fruit. *Tea:* tea with milk (no sugar), 2 oz. salt-free bread, ½ oz. salt-free butter, 4 oz. fruit. *Supper:* 4 oz. white fish, 5 oz. root vegetables, salad (2 oz. lettuce, 3 oz. tomato, 1 oz. watercress), 2½ oz. salt-free bread, ½ oz. salt-free butter, 4 oz. fruit. *Bed-time:* any milk left from 1½ pints. Alterna-

*One ounce avoirdupois = 28.4 g. One fluid ounce = 28.4 ml.

tives for lean beef are: lean mutton, lean veal, liver, heart, rabbit, chicken, rationed cheese (cheddar type). Calcium, iron, and vitamin supplements (A, B complex, C, D) are necessary. The actual vitamin content of fruits and vegetables is always doubtful. Food yeast, which is a good source of vitamin-B group, can be used to improve the flavour of the skimmed milk.

Once pregnancy toxaemia has established itself the following 1,200-calorie diet should be advised: 1 pint skimmed milk daily. *Breakfast:* tea or coffee with milk (no sugar), 1½ oz. salt-free bread, ½ oz. salt-free butter, 1 egg, 4 oz. fruit or tomato. *Mid-morning:* tea or coffee with milk (no sugar). *Lunch:* 2 oz. lean beef or equivalent (see 1,800-calorie diet above), 6 oz. green vegetable, 5 oz. root vegetable, ½ oz. margarine for vegetables, 4 oz. fruit. *Tea:* tea with milk (no sugar), 1 oz. salt-free bread, ½ oz. salt-free butter, salad if desired. *Supper:* 4 oz. white fish, salad (2 oz. lettuce, 3 oz. tomato, 1 oz. watercress), 1½ oz. salt-free bread, ½ oz. salt-free margarine, 4 oz. fruit. *Bedtime:* any milk left from 1 pint. Protein, mineral, and vitamin values cannot be increased without increasing calorie value, except by the use of concentrates and supplements. Skimmed milk is recommended as a means of maintaining protein and calcium levels in this calorie intake. A protein supplement, such as a casein preparation, can be added to the milk. The usual vitamin supplements will be required, and food yeast, which can be given to improve the flavour of the skimmed milk, is a good source of vitamins of the B group. Calcium and iron supplements are necessary. With a diet restricted to this degree it is advisable for the patient to be in bed. After a week, depending on the patient's condition—weight loss, blood pressure, albuminuria—it might be possible to increase the calorie intake to 1,500 calories.

R. H. J. Hamlin has recently reported that in a large maternity hospital in Sydney eclampsia has been eliminated and pre-eclampsia reduced to a minimum by the adoption of two simple measures: (1) The giving of correct diet education in the early weeks of pregnancy (low-carbohydrate, high-protein, high-vitamin diet before mid-pregnancy). (2) Restricting the mother's increase in weight to 8 lb. between the 20th and 30th weeks of pregnancy.

Bat Ears

Q.—*What is the optimum age for operating on a protruding ear? The patient in question is a child aged 20 months with marked protrusion of both ears.*

A.—Operative correction of protruding ears is best delayed until the child is at least 4 years old. In cases of marked protrusion it is desirable to perform the operation before the patient starts school. With mild deformities the operation is best left until the age of 9 or 10 years. In early childhood there is disproportion between the size of the ear and the size of the head, and mild degrees of protrusion may become less obvious as the child grows.

Heliotherapy

Q.—*What are the therapeutic uses of sunshine? Can different effects be obtained from it, especially in the Tropics or subtropics, by exposure at different times of the day?*

A.—The solar spectrum includes ultra-violet and infra-red rays which are used therapeutically. The ultra-violet rays will cause pigmentation, but the actual medical value of these rays is not very great. The infra-red rays (or heat rays) are widely used in therapy. Strong sunshine can therefore be used as a substitute for an infra-red lamp. The only difference that the time of day would cause in treatment is that the amount of rays would decrease as the sun drops towards the horizon. Attempts have been made to set up solaria in places such as the South of France for the therapeutic use of the sun spectrum, but in actual practice it is usually more certain and convenient to use artificial methods of producing these rays rather than to depend on the vagaries of the weather.

Storage of Drinking-water

Q.—*How may water in storage tanks be kept fresh for drinking? I wish to store water in a 10-gallon (45.5-litre) galvanized container for periods up to a fortnight.*

A.—The tank should be provided with a lid which excludes light and dust. It should be cleansed and then sterilized as follows: Half-fill with tap water; add 3 oz. (85 ml.) of a 1% solution of chlorine; completely fill with water; see that the under-surface of the lid is also cleansed with chlorine solution and do not allow it subsequently to become contaminated; replace lid; allow to stand for 24 hours; empty tank. (This need not be repeated each time the tank is filled unless there is good reason for doing so.) The tank may then be filled with tap water, after making sure that any hose used for this purpose is clean. The lid should then be carefully replaced to exclude light and dust. Should there be any doubt about the purity of the water a teaspoonful of 1% chlorine solution may be added while filling the tank. The tank should be situated in as cool a place as possible. Water stored in this manner should keep sweet and pure for at least one month.

The Doctor at the Sink

Q.—*In reply to a question on cleaning empty medicine bottles (August 11, 1951, p. 371) liquor sulphestolis B.P.C. was recommended. Would this substance be equally useful for domestic dish-washing?*

A.—Liquor sulphestolis *B.P.C.* is quite satisfactory for the washing of kitchen utensils, being particularly effective in removing grease. It also gives a good polish to glassware. If the vessels are thoroughly rinsed afterwards there is unlikely to be any noticeable smell and practically no danger of toxicity. Liquor sulphestolis is available commercially under various trade names.

NOTES AND COMMENTS

Pregnancy Tests.—Dr. H. BERIC WRIGHT (London) writes: It does not seem to be generally realized that the Hogben test is at least as reliable as the better-known Aschheim–Zondek and Friedman tests ("Any Questions?" March 1, p. 501). This is a pity, because this method has advantages both for the practitioner and for the pathologist. Landgrebe and Hobson (*British Medical Journal*, 1949, **2**, 17) showed that the Hogben test is, if anything, more accurate than the Aschheim–Zondek. It has the advantage—to the practitioner—of giving a result within 24 hours of receipt of the specimen. Thus a laboratory using this method can give a more rapid service than one using the Aschheim–Zondek or Friedman technique. The test usually becomes positive within 10 to 14 days of the first missed period. From the point of view of laboratory technique the animals used for the Hogben test are easier and cheaper to keep and can be used repeatedly. The Hogben test is thus to be preferred by both the practitioner and the pathologist and deserves to be more widely recognized than it is at present.

OUR EXPERT writes: It is true that the pregnancy diagnosis test using the female toad *Xenopus laevis* has certain advantages over the Aschheim–Zondek and Friedman tests; still further advantages are possessed by the Galli Mainini test using male amphibia such as *Bufo arenarum* Hensel, *Rana pipiens*, and *Rana esculenta*, for in these tests the result is obtained in less than three hours.

Correction.—In a reply to a question on hair oil ("Any Questions?" March 15, p. 614) reference was made to R. C. Harry's book *Modern Cosmeticology*. This is published by Leonard Hill Ltd., *not* by Chapman and Hall as stated.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499 TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
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